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> *Of nature trusts the Mind that builds for aye*"—WORDSWORTH

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PRESERVATION OF THE COUNTRYSIDE IN BRITAIN

THE two outstanding features of the year covered by the ninth annual report of the National Parks Commission* have been, in the Commission's own judgment, a series of Acts of Parliament with a direct bearing on its work, and Ministerial decisions on three extensive development proposals in national parks in Britain. Referring specifically to major industrial developments in the Pembrokeshire Coast National Park and the decision to sanction the construction of a nuclear generating station at Trawsfynydd in Snowdonia, the Commission affirms that, if it is to discharge the responsibilities which Parliament has entrusted to it, it must increasingly strive to ensure that every possible alternative site has been fully considered before permission is granted for such developments in a national park. It is reluctant to believe that, although it has been decreed in the over-riding national interest that particular major industrial undertakings shall be permitted in national parks, this signifies that national parks are being devalued as a national asset by those with whom the ultimate responsibility for these decisions rests.

Scant reassurance, however, on this point is to be found in the debate in the House of Commons on January 30 on the National Parks (Amendment) Bill introduced by Mr. A. Blenkinsop, though reference was freely made to the Commission's report in that debate; and it is in the light of that debate that the bearing on the Commission's work of the Acts in question—the Land Powers (Defence) Act, the Litter Act, the Local Government Act, the Milford Haven Conservancy Act and the Opencast Coal Act—is best appreciated. In so far as some of these likewise bear on the work of the Nature Conservancy†, a similar remark might apply to the ninth report of the Conservancy. Except against that background, the record of quiet but steady progress recorded in these two reports could engender an optimism that is quite unjustified and out of keeping with what remains to be done and the real national needs in regard to amenity and conservation.

Mr. Blenkinsop's Bill was opposed by the Minister of Housing and Local Government, Mr. H. Brooke, who pointed out quite rightly that the Bill was, in effect, a Financial Bill and that Parliament does not accept Private Members' Bills which propose the expenditure of public money. It is the tradition of the House that it should be the Government which shall choose and decide which proposals for additional expenditure should be placed before Parliament. Because of this principle, which is independent of the merits of the detailed provisions of the Bill from the point of view of the national parks, Mr. Brooke did not examine the Bill further. Most of its recommendations are, in fact, based on recommendations made to the Ministry by the Commission or by the County Councils Association; but in directing attention to this principle, Mr. Brooke placed the responsibility for the financial difficulties of the national parks in Britain fairly and squarely where it rests—with the Government.

There has never been any adequate financial provision made for the work of the National Parks Commission, either for its positive and constructive activities or even for its ordinary administration, largely because the burden of serving a national interest has been placed on the constituent counties, some of which are financially very weak. It is not, therefore, sufficient for Mr. Brooke to decline to undertake that the Government would introduce a Bill on the subject. If the idea of national parks is to have any real meaning, the Government must give serious consideration to their financial position and take early and adequate steps to meet their needs: a need which indeed is accentuated by the other grave threat to the whole conception—that of development. To concert the measures which keep the damage from development to a minimum usually demands much negotiation, consultation, and examination of sites, all of which costs money, and taxes to the limit the resources of the Commission and the other amenity societies.

Mr. Blenkinsop indicated clearly enough the minimum requirements. Less than £100,000 a year is being spent on the national parks of Britain, in the areas themselves or in the offices of the Commission. In the first place he proposed, in accordance with the Commission's own request, that the Minister's powers of providing grants should be widened to include any work done by the national park authorities under the broad enabling powers of the principal Act. This, in practice, would, for example, permit grants for such purposes as providing information centres in the parks, publicity action, anti-litter campaigns, etc. Secondly, he suggested the removal of those restrictions upon the powers of the Commission which prevent it from carrying out work which is the statutory responsibility of some authority but which (again often for financial reasons) is not being discharged. Thirdly, he strongly urged that, as recommended both by the Commission itself and the County Councils Association, the Minister should be allowed to make grants for the administrative expenses of the parks.

There were other minor suggestions in relation to the long-distance footpaths, the provision of wardens and making planning authorities responsible for the creation of new rights of way and their maintenance in national parks; but although the debate was poorly attended the Bill had support from all sides of the House of Commons, and it focuses attention on the neglect of the Government, when the Act was originally passed and since, to provide the financial resources without which the purpose of the Act cannot be achieved. The Commission itself made further representations to the Minister during the year regarding the need for early amendment of the Act, but in his reply of April 11, 1958, Mr. Brooke held out no hope of Parliamentary time being available for a Bill on this subject. The Nature Conservancy is more restrained in its comments on financial needs, but the report makes it clear enough how far its scientific work and the management of the reserves are limited by lack of funds. The recommendation of the Select Committee on Estimates that "Ways and means should be sought for strengthening the Conservancy's liaison with the universities and for increasing the contribution to scientific research to be expected from them" is warmly welcomed.

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* National Parks and Access to the Countryside Act. Ninth Report of the National Parks Commission for the year ending September 30, 1958. Pp. iv+79+8 plates. (London: H.M. Stationery Office, 1958.) 5*s*. 6*d*. net.

† Report of the Nature Conservancy for the year ended 30th September, 1958. Pp. vi+119+14 plates. (London: H.M. Stationery Office, 1958.) 6*s*. 6*d*. net.

The National Parks Commission in the present report also refers to the Land Powers (Defence) Act, 1958, concerning which the Commission was consulted, and in which provision was made that military manœuvres commissions should include, in addition to a member nominated by the Commission, "at least one person appearing to the Minister to be specially qualified to watch over the amenities of the areas in which the manœuvres are to be held". The Commission also welcomes the provision in the Act which empowers Service Ministers to use land occasionally for training and minor exercises, and thus enables them to reduce their holdings. The Litter Act, which received Royal Assent last July, is also regarded as a big step forward in the campaign against litter ; but it could well increase the financial needs of the Commission if the Act is to be made effective. The Local Government Act, 1958, leaves undisturbed the existing grants to local authorities under the National Parks and Access to the Countryside Act, 1949, but it is welcomed as a recognition of the national interest in national parks and in areas of outstanding natural beauty and as leaving the way open for extending these grants. While regretting, however, that further provision for opencast coal operations is made in the Opencast Coal Act, 1958, the Commission welcomes the improved safeguards for amenity contained in the Act.

These provisions follow corresponding sections in the Electricity Act, 1957, and the Milford Haven Conservancy Act, 1958, and these sections are heartening examples of the greater concern for the preservation of amenity which is now felt both in Parliament and in Britain generally. While it is true that the work consequent on the passing of the Town and Country Planning Act of 1947 and the National Parks and Access to the Countryside Act of 1949 has had a beneficial effect on the landscape, and that the cumulative effects of planning control have been considerable, the very passage of these new Acts and the granting of Ministerial consent for development proposals in national parks which have caused such disquiet to the Commission show the extent to which the effectiveness of its work lies largely outside its control. It depends on the amount of support which the Government is prepared to give for both amenity and conservation, at least in limited and specified areas, as an over-riding national interest, and to provide the financial and other resources to maintain that interest in the face of either departmental or sectional or local interest. That in turn ultimately depends on the development of an informed public opinion, alert to support the study work of planning authorities, within and outside national parks, and determined to safeguard with intelligent care the traditional and most vulnerable and often irreplaceable beauty of the countryside of Britain.

NEW ASPECTS OF THE GENETIC CONTROL OF INDUSTRIAL MELANISM IN THE LEPIDOPTERA

By DR. H. B. D. KETTLEWELL
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AN absolute necessity to achieve dark coloration in order to preserve crypsis and survive has, in the past hundred years, confronted a large number of species of moths. County lists bear witness to the fact that some have failed and have been driven out of urban areas and their surroundings : the requisite mutations have not taken place in time. In at least two species (*Procus literosa* Haw. and the *Apamea characterea* Hb.), we have evidence that, after local extinction, an urban area has later been repopulated by melanic forms of the same species[1]. Until recently, we had assumed that successful industrial melanics had nearly always come about by the successful mutation of single dominant melanic genes, which, in one step, changed the insect from white to black[2].

In *Biston betularia* L., the peppered moth, I have shown by mark–release–recapture experiments that the cryptic advantage derived from this colour-change could alone account for the spread of industrial melanism[3]. Nevertheless, it has also been shown that, apart from colour, there are profound behavioural and physiological differences[4,5]. I have postulated theories based on the fact that melanic mutants, dominant in the few known instances and similar in every way to those spreading to-day throughout the industrial areas of the world, are to be found in moth populations, frequently as a balanced polymorphism, in many parts of the world remote from the effects of industrialization : the Caledonian forests of Scotland ; the sub-Arctic of Canada ; and the rain forests of South Island, New Zealand[6]. I have suggested that this same basic one-gene switch-mechanism has probably been used in the past for very different reasons when blackness conferred advantage[7] ; for the assimilation of heat in cold climates; in dark rain forests; or possibly before deciduous trees succeeded the conifers in the northern hemisphere. In this instance, then, the 'pre-adapted' gene of Cuénot[8] is seen, not as a fortuitous happening, as has recently been suggested[9], but as a mechanism fulfilling recurring, though differing, needs which have from time to time been demanded for periods in the past history of a species. During these periods dominance has been achieved by natural selection.

Apart from this mechanism, we are finding evidence that others exist to promote darkness. One of these involves the use of polygenes, which bring about the gradual darkening of a normal population. There are certain species of Lepidoptera that have failed to mutate to a successful dominant melanic but have continued to survive in their typical form in urban areas. It has been repeatedly noted that, when these 'typicals' were compared with rural forms of the same species, the urban populations were much the darker. For example, *Gonodontis bidentata* Cl., which does not fly actively, has a single dominant black mutant, form *nigra* Prout. On Cannock Chase outside Birmingham, this comprises more than 50 per cent of the population. In central Birmingham, however, that mutant does not occur, but the typical specimens, which still survive there, are darker than their normal forms elsewhere. A large number of species in Sheffield, London and elsewhere fall into this category.

It is interesting to reflect on whether these darkening genes are the same as those which are responsible for blackening the heterozygotes of unifactorial melanics. We have previously recorded that the earliest heterozygotes of *B. betularia*, extracted from collections made in the past century, are different from the majority of specimens collected recently[10]. They were in fact somewhat intermediate in character, with varying degrees of white markings on the wings—a condition rarely found to-day. *B. betularia* form *carbonaria* now has complete dominance, the heterozygotes being indistinguishable from the homozygotes in the majority of individuals. Dominance has been achieved by the selection of modifiers in the gene-complex. Present indications are that in *B. betularia* many of these modifiers are not the same: the few remaining recessive typicals occurring in Birmingham are more variable, but not on an average darker, than rural ones. Probably the insect is so white, anyway, that it has not had the opportunity of mobilizing its polygenes for darkening, because the white form is always conspicuous in urban areas. Selective predation between typical individuals has, therefore, not taken place: they are eliminated indiscriminately. They continue to appear because of the advantage of the heterozygous *carbonaria* in the population.

Apart from the polygenic form, we encounter other modifications of the inheritance of melanism. In north Germany, *Lymantria monacha* L. has a gradation of phenotypes from white to black. The blackest (f. *atra* Linslow) is the result of three dominant genes (one sex-linked). Melanics of multifactorial origin are, surprisingly, uncommon in the Lepidoptera.

Sex-limited melanics, found in the female only, are known in a few species (*Phigalia pedaria* Fab.)[11], though whether the gene is in the Y-chromosome, or inherited cytoplasmically, has not at present been ascertained.

Until recently, I had repeatedly stated that no example was known of a *recessive* melanic mutation having spread: that recessive melanics were always rare, sub-viable and for the most part limited to non-cryptic species in which black forms, in past periods, had never been of use to the species[12]. This remains substantially true, but we have now found one: the bombycid moth, *Lasiocampa quercus* L., the oak eggar, and its two dark forms, which are increasing rapidly. One is green-black, *olivacea* Tutt (*olivaceofasciata* Cockerell), to which, until recently, all melanic *quercus* were referred. The other, *lurida* Cockayne[13], recognizably different when freshly hatched, is red-black. It seems likely that the two forms are modified expressions of the same recessive gene, or possibly they are alleles.

The oak eggar, in its northern form *callunae*, at times swarms on the heavily polluted Yorkshire moors. Unfortunately, it has a two-year life-history, the larva occurring in even years only and the moth in odd. In a sample of 493 moths collected in 1957, 23 (4·7 per cent) were of the dark recessive forms, so that about a third of the population were heterozygotes assuming equal viability of the genotypes. At present we cannot identify these with certainty, but there is evidence that a majority of the typical population are darker to-day than they were twenty years ago. Similarly, present-day melanics are darker than the earliest specimens taken from the same moor when they formed about 1 per cent of the population (though they do not fade).

A further interesting point in regard to form *callunae* is that, in Yorkshire, about 4 per cent of the wild larval population are black (82 in a random sample of 2,000 in 1956) though normally they are yellow-brown in colour (Fig. 1). They are hairy but are predated by cuckoos. A proportion (about 50 per cent) of the black larvæ produce black moths, as do a very much smaller proportion (less than 2 per cent, 1956) of yellow-brown larvæ. Natural selection, working on partial linkage between the genes controlling black larval and imaginal colouring, is the most probable explanation of the situation[14]. We are at present testing the cross-over values both in this locality and in other places where the same phenomenon occurs.

The female of the oak eggar, an insect of great size, is typically pale yellow. It hatches in the daylight hours and sits on heather stems, rarely flying except at night. The males, which are chocolate brown with bright yellow conspicuous bands, particularly on the underside, assemble in great numbers to them. The males, therefore, fly actively, in fact wildly, by day. To the human eye, form *olivacea* females were invisible on their backgrounds at, on an average, more than seventeen yards. The yellow female, on the other hand, was still visible at fifty-seven yards.

During the summer of 1957 we undertook an intensive study of this moth on Rombolds Moor, in June, where it was abundant. This is part of Ilkley Moor and is within fourteen miles of Bradford, Leeds and Skipton. The heather, walls and even the ground itself were black with pollution. Each day we observed large flocks of black-headed gulls (*Larus ridibundus* L.) flying slowly over the heather and dropping into it every few yards as they gorged themselves on the female eggars. The black-headed gull has only comparatively recently, in the past thirty years, extended its summer range to central England. Because of the insufficiency of melanic females, we were unable to undertake extensive mark-releases, comparable with those we had previously carried out on the peppered moth. On one occasion,

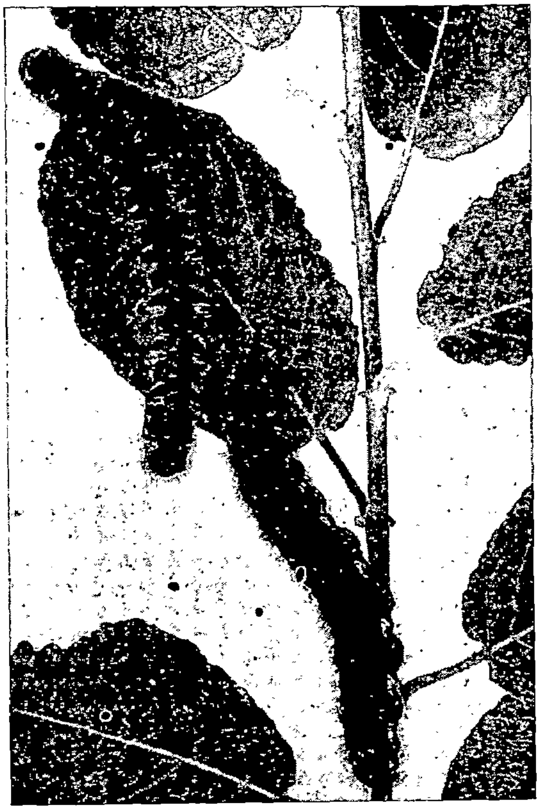

Fig. 1. Full-grown larvæ of *Lasiocampa quercus* L. Upper, normal yellow-brown colour; lower, melanic larva

however, of forty-six moths released, forty-four typical and two form *olivacea*, one *olivacea* was the only moth left after 2 hr. This suggests a very large visual selective advantage for the recessive dark mutant. Predation was so intense that few females could be seen at the end of a day, and the following year, in 1958, 134 larvæ only were found in a week compared with more than two thousand in a few hundred square yards during searching for 24 hr. in 1956 on precisely the same area.

Male eggars were also taken on the wing by the gulls and we observed swifts (*Apus apus*) catching them in numbers as well as wheatears (*Oenanthe oenanthe*). To us the melanic males were much more difficult to follow in flight than male f. *typica*. This was probably due to the absence of yellow bands, apart from their black colour (Fig. 2). We were also able to examine the 'feathering ground' of a pair of merlins (*Falco columbarius*) which were feeding extensively on the male moths. No melanic wings were present among the five dozen wings collected.

The dark mutants are to-day found throughout the industrial Yorkshire moors. Near Wallasey in Cheshire, form *olivacea* also occurs in about 5 per cent of the population, but here it has a one-year life-history[15]. In Caithness, northern Scotland, it constantly recurs in the population but is not so dark as elsewhere. In the rest of Britain it is a very rare mutant. Near Brandenburg in East Prussia, a similar or identical black mutant to f. *lurida* occurs near the estuary of the River Haval, and it is stated that it constitutes 100 per cent of the population, forming a local race[16]. 100 per cent of the caterpillars bred from this stock were also of the black form.

We have been able to collect further evidence on the spread of the recessive melanic in Britain. W. E. Collinson[17] has studied this insect in Yorkshire since 1936. He has observed the increasing frequency of the melanics which at that time formed about 1 per cent of the population. He has noted that the average colour of the typicals is getting steadily darker in this population, and he has observed the gradual darkening of the dark forms during the past twenty years. Moreover, he has recorded violent fluctuations in population size.

In 1957, I released 693 marked males and, using assembling traps placed over a square mile, recaptured 33 in a sample of 478 caught on subsequent days. This gives an approximate total male population of 10,000 for the peninsula of moorland on which I was working. There had taken place, therefore, a very high mortality-rate from the prodigious larval population of the previous year, 1956, when they swarmed in their thousands. A random sample of 311 cocoons picked up suggested the following pupal death-rate alone, regardless of late-larval mortality:

(1) Normal hatching		43
(2) Magpie predation. These have been observed to feed upon the pupæ in winter		81
(3) Disease. Virus and fungi. Unknown causes		170
(4) Parasites. Living solitary Ichneumonidae larvæ (1948)	4	= 17
Hatched Ichneumonidae	13	

This reflects a pupal mortality-rate of approximately 86 per cent. Of the total pupal population, therefore, 26 per cent were eliminated due to visual predation by magpies, and here it must be recorded that the *black* larvæ produce *black* cocoons, which are much more difficult to see than those of the typicals. Unfortunately, I was unable to recognize the differential predation on the cocoons because of bleaching.

We have then a situation in which two recessive melanic genes are spreading through a population. One controls larval colour, which is also reflected in the colour of the cocoon. The other is responsible for imaginal coloration. It seems that the genes for both are partially linked both in the Yorkshire and Cheshire localities. In Caithness, where *L.* f. *olivacea* forms a proportion of the population, the black larvæ do not occur[14]. The same situation is found in restricted areas in Holland and Denmark[18]. On

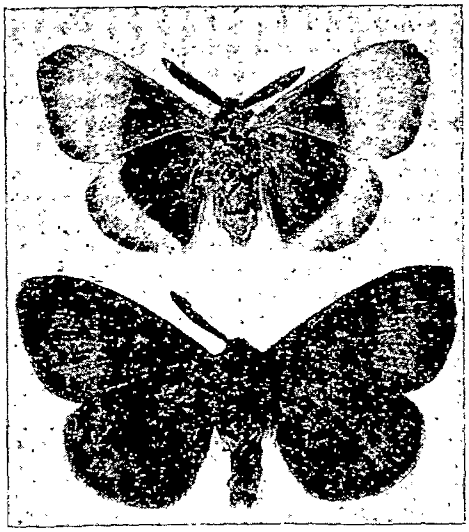

Fig. 2. *Lasiocampa quercus* L. f. *callunae*. Undersides of two males. Upper, f. *typica*; lower, a recessive melanic *lurida* Cockayne

the other hand, in Prussia there is evidence that a local population exists of black moths with black larvæ, though this is doubted by Cockayne[14].

We have worked on one other species in which larval and imaginal melanism is associated, the only other example known to me. *Arctia caja* L., the garden tiger moth, normally has crimson hind-wings which are only displayed on attack. There is a variable brown hind-winged form, *brunnescens* Stattermayer, which is the heterozygote of an all-black individual form, *fumosa* Hörhammer ; it is therefore incompletely dominant. All *fumosa* so far have been bred from black larvæ. The heterozygous larvæ are indistinguishable from those of typical *caja*, and this character, therefore, suggests that the same gene is responsible for both larval and imaginal coloration.

It will be of the greatest interest to see whether in the Yorkshire black eggars, natural selection, working on the cross-over value, will eventually bring the two genes for larval and imaginal melanism so close together that they act effectively as a single supergene. This would contrast with the situation in *Arctia* *ja*, where we feel confident that the association between black colour in larva and imago respectively has not been produced in this way. For here we are dealing with a very rare mutant, which has had no history of favourable selection necessary to bring two originally separate but advantageous genes together to form a controlling unit.

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CÆSIUM-137 IN DRIED MILK

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THE presence in human beings of traces of cæsium-137 derived from the world-wide fall-out of fission products from nuclear weapon tests was first reported by Miller and Marinelli[1] in 1956, and was also observed in human subjects in Britain by Rundo[2]. The main source of cæsium-137 in humans is probably cow's milk[3]. This article discusses the results of measurements of cæsium-137 and potassium in dried milk collected from different parts of the United Kingdom during 1957 and the first half of 1958. Measurements of the cæsium-137 and potassium contents of hay from four of these localities are also reported.

Samples of dried milk have been obtained from nine different areas in Great Britain, and studied for cæsium-137 and potassium content. Dried milk from one area has been studied since early in 1955, while most of the remaining samples were collected between April 1957 and June 1958. Table 1 gives the details of the factories, milk-collecting areas, the type of dried milk sample and the villages from which samples of hay were collected.

Estimation of Cæsium-137 and Potassium

Gamma-scintillation spectrometry was used for estimating potassium and cæsium-137 in dried milk with the aid of a sodium iodide crystal 3 in. diam. × 3 in. high with a photomultiplier and a five-channel pulse-amplitude analyser. Cæsium-137 was estimated from the 0·662-MeV. gamma-ray emitted by its short-lived daughter barium-137-*m*[4] ; potassium-40 occurs naturally in potassium and emits a gamma-ray of 1·46 MeV.[4]. Counting rates in the two photopeaks from a 2-kgm. sample of dried milk were compared with those from a similar standard sample of dried milk containing additional standardized cæsium-137 and another sample containing added potassium. A few dried-milk samples of only 500 gm. weight were measured with less accuracy.

The activity in hay samples was measured with the co-operation of Dr. J. Rundo of the Health Physics Division, Atomic Energy Research Establishment, using a gamma-spectrometer designed for monitoring the human body. This instrument utilizes four sodium iodide crystals 4 in. in diam. × 2 in. high. Counting rates were observed on a 100-channel pulse-amplitude analyser, and were compared with those from a sack of hay containing added standard cæsium-137 sources, and a sack with potassium chloride added. The hay, which was harvested

Table 1. MILK- AND HAY-COLLECTING AREAS

Factory	*Milk-collecting area*	*Type of sample*	Hay sampling sites
Buckingham	North Buckinghamshire, South Northamptonshire	*F* and *S*	—
Carlisle	East Dumfriesshire, North Cumberland	*F* and *S*	Little Orton, Unthank, Dalston, Rockcliffe, Kirkbride
Carmarthen	Carmarthenshire	*F*	Llangain, Llanstephan, Conwil Elvet, Newchurch, Llanwinio
Coleraine	Counties Antrim, Fermanagh, Londonderry and Tyrone	*F*	—
Congleton	North Staffordshire, Cheshire	*F*	—
Driffield	East of North Riding, North of East Riding	*F*	Kilham, Wintringham, Nafferton, Scagglethorpe, West Heslerton
Frome	East Somersetshire, West Wiltshire	*S*	Leigh-on-Mendip, Holcombe, Binegar, Stratton-on-the-Fosse, East Horrington
Garstang	North Lancashire	*F* and *S*	—
Mauchline	South Ayrshire	*S*	—

F, dried full-cream milk ; *S*, dried skimmed milk.

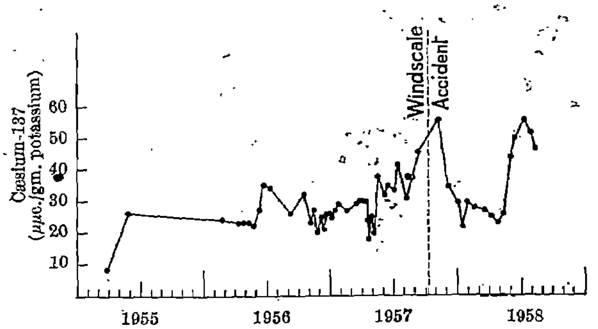

Fig. 1. Cæsium-137 in dried milk (Frome)

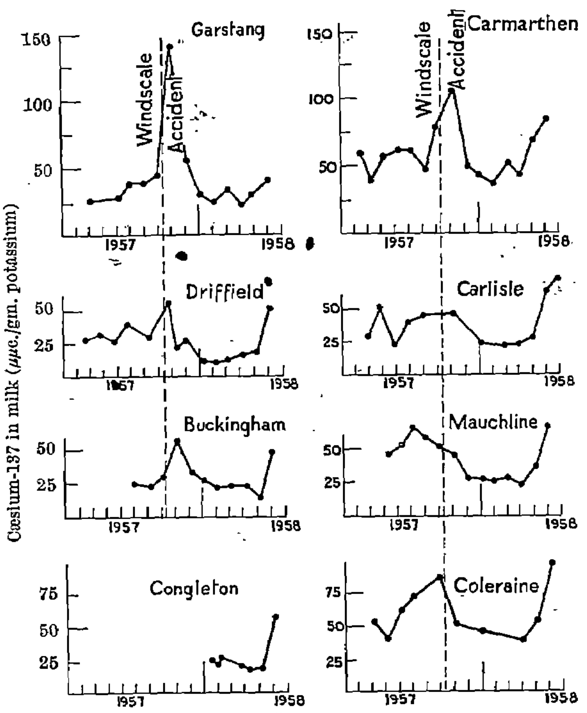

Fig. 2. Cæsium-137 in dried milk

in the summer of 1957, was measured in July 1958. This delay allowed the zirconium-95 which has a radioactive half-life of 65 days to decay by a factor of about fifty. At this time the gamma-rays of about 0·75 MeV. from zirconium-95 and its daughter niobium-95[4] did not mask the peak at 0·662 MeV.

Cæsium-137 and Potassium in Dried Milk

The cæsium-137/potassium ratio in dried skimmed milk manufactured in Frome, Somerset, has been plotted in Fig. 1 for the period 1955–August 1958; the results to January 1957 have already been published[5]. Fig. 2 gives the results for the cæsium-137/potassium ratio in dried milk from other areas. The measurements show that there is little, if any, variation in the potassium content of dried milk either with time or location. The average values obtained are 15·4 gm. potassium per kgm. dried skimmed milk, and 11·3 gm. potassium per kgm. dried full-cream milk. The probable error of counting on these measurements is ± 0·3 gm. of potassium per kgm. of dried milk. On the cæsium-137/potassium ratio the probable error of counting is ± 2 μμc./gm.

From Figs. 1 and 2 it is seen that there is an apparent seasonal variation in the cæsium-137/potassium ratio. The decrease in the winter may be due to the change in the feeding habits of cows during winter, when they are given supplementary food. Samples from all areas show an increase in the cæsium-137/potassium ratio in June 1958. The rise at this time of year is associated with cows going out to pasture in the spring; but the levels observed are enhanced by the higher than usual rate of fall-out at this time from nuclear test explosions[6]. In the only area from which samples have been measured beyond June 1958, it seems that the cæsium-137/potassium ratio reached a maximum in July 1958.

Average values of the cæsium-137/potassium ratios have been taken for each of the eight areas where results are available from April 1957 to April 1958. Samples collected in late October and November have been excluded (see next section). The average ratios have been plotted against the average annua rainfall in inches for each area in Fig. 3. There is an apparent correlation between the cæsium-137/potassium ratio in dried milk and the annual rainfall. T slope of the line in Fig. 3 gives a value for the rati

$$m = \frac{\text{Cs-137/K ratio in milk } (\mu\mu\text{c./gm.})}{\text{annual rainfall in inches (in./year)}}$$

For the United Kingdom the value of m was 1 for the period April 1957–April 1958. A simil correlation between the cæsium-137/potassium rati in milk and the annual rainfall has been observe by Anderson[3] in the United States, with values o m of 1·9 and 0·7 for two different parts of the United States.

Effect of the Windscale Accident

Inspection of Figs. 1 and 2 shows that dried milk from all collecting centres south of Windscale (Buckingham, Carmarthen, Driffield, Frome and Garstang) showed an increase in the cæsium-137/potassium ratio for the first sample manufactured after October 10, 1957, while the other samples (Carlisle, Colerai and Mauchline) showed a decrease in the rati. The largest increase, of 95 μμc./gm., was in the dried milk from Garstang (the significance of these measurements of the cæsium-137 content of dried milk can be judged from the recommendations regarding the permissible intake in emergencies made to the Medical

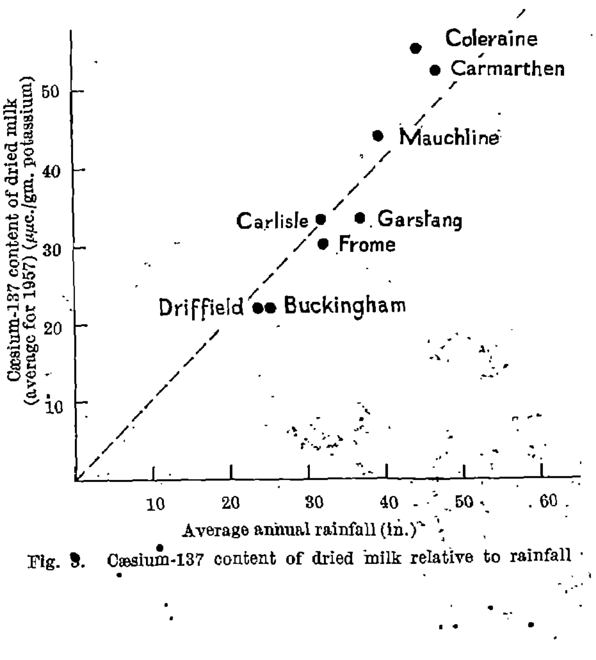

Fig. 3. Cæsium-137 content of dried milk relative to rainfall

Table 2. Cæsium-137, Potassium, Strontium-90 and Calcium Content of Hay (1957)

Location	Cs-137	K	Cs-137/K	Sr-90	Ca	Sr-90/Ca
	μμc./kgm.	gm./kgm.	μμc./gm.	μμc./kgm.	gm./kgm.	μμc./gm.
Carlisle	450	14·2	32	260	4·5	57
Carmarthen	870	8·8	99	530	5·3	100
Driffield	460	17·8	26	290	6·5	44
Frome	650	15·0	43	340	4·2	80
Probable errors of counting	± 70	± 1				

Table 3. Activity Ratios in Hay and Milk

Location	Cs-137 in hay	Cs-137 in milk	Observed Ratio	Sr-90 in hay	Sr-90 in milk	Observed Ratio
	μμc./gm. K	μμc./gm. K		μμc./gm. Ca	μμc./gm. Ca	
Carlisle	32	35	1·1	57	4·8	0·08
Carmarthen	99	61	0·6	100	7·5	0·08
Driffield	26	30	1·2	44	4·6	0·10
Frome	43	38	0·9	80	5·5	0·07
Average			0·95			0·08

search Council by the Council's Committee on otection against ionizing radiations (*Brit. Med. J.*, the press)), which is the station nearest Wind-ale, and is in the line of the plume of activity ich was released in the accident[7,8]. Garstang is out 70 km. from Windscale.

Mayneord *et al.*[9] have studied milk from Cardigan-ire during the period of the Windscale incident, and ve shown that the cæsium-137/potassium ratio creased from 80 μμc./gm. to more than 300 μμc./gm. day or two after the accident. By early November the ratio had decreased to about 150 μμc./gm., which is similar to the result of 107 μμc./gm. given in Fig. 2 for Carmarthen milk dried on November 5.

Using figures quoted by Booker[10] for the ratio of iodine-131 to cæsium-137 activities in herbage near Windscale, and the figures for the deposition of iodine-131 on herbage in North Lancashire, the deposition of cæsium-137 in the Garstang area can be estimated as 15 mμc./sq.m. of herbage. This corresponds to an rease of about 100 per cent on the previously isting cumulative cæsium-137 fall-out in this area rom distant bomb tests[6,11]. (Gustafson *et al.*[12] have easured the cæsium-137 content of soil from Braidwood, Illinois, which was collected in October 1957. They find 14·3 mμc. of cæsium-137 per sq.m. of soil from an area which has approximately the same rainfall as Garstang.) However, the cæsium-137/potassium ratio in dried milk from Garstang in June 1958 was as low or lower than that in dried milk from other areas. These facts are consistent with the hypothesis that most of the cæsium-137 which appears in dried milk comes from direct fall-out on the herbage and little from the soil. A similar conclusion was tentatively reached by Anderson[3].

Cæsium-137 and Strontium-90 in Hay and Milk

Hay from the 1957 crop was collected from four areas corresponding to four of the areas from which dried milk was collected. In each area a sample of hay was collected from each of five farms (in villages named in Table 1) and the samples were mixed. Table 2 gives a list of results of the cæsium-137 and potassium analyses of the hay samples. Also included are the results of the strontium-90 and calcium analyses performed on the hay samples by Bryant (private communication). The cæsium-137/potassium nd strontium-90/calcium ratios appear to be correated with each other and are of the same order of agnitude.

In Table 3 the cæsium-137/potassium and strontium-90/calcium ratios in the hay samples are compared with the same ratios in dried milk averaged over the period June–September 1957. The results for the strontium-90 and calcium in milk are quoted from Bryant *et al.*[13]. The ratio of the results for milk and hay have been included under the heading "Observed Ratio" (Comar *et al.*[14]). In using this term the following assumptions have been made: (1) The five farms from which the hay was taken were representative of all the farms sending milk to the collecting centres. (2) The grass cut for hay in the summer of 1957 was representative of the grass eaten by the cattle during June–September 1957 in respect of the cæsium-137/potassium and strontium-90/calcium ratios. (3) The cæsium-137/potassium and strontium-90/calcium ratios in the milk of the cows were representative of their feed at that time; that is, the milk was in equilibrium with the diet.

Of these assumptions (2) is probably the most doubtful, since the grass grown for hay would have a longer exposure to foliar uptake than that grazed continuously. During the summer of 1956, Bryant *et al.*[15] compared the strontium-90/calcium ratio in the accumulated growth of grass with that in which the grass had grown for only three weeks since the plot was last cut. This was done periodically during the summer at four stations. The accumulated growths had an average of only 28 per cent more strontium-90 per gm. of calcium than the new growth, which suggests that the error in taking accumulated growth would not be very large.

The assumptions are also supported by the fact that the Observed Ratios for the strontium-90/calcium ratios given in the last column of Table 3 lie not far outside the range of those reported from more carefully controlled experiments[14]. In particular, Morgan *et al.*[16] found an Observed Ratio of 0·09 for the strontium-90/calcium ratio in passage from diet to milk for a herd of cows at Sonning, Berkshire.

The Observed Ratio for the cæsium-137/potassium ratio varies considerably from region to region (from 0·6 to 1·2), but there is a clear indication that this ratio is near unity; this is very different from the Observed Ratio for the strontium-90/calcium ratio, which is about 0·1.

A qualitative comparison can be made with the cæsium-137/potassium ratios in human beings. Rundo (private communication) has found an average cæsium-137/potassium ratio of 45 μμc./gm. in individuals from Oxfordshire and Berkshire in the latter half of 1957. This result is not significantly different from the ratios in hay and milk from Frome, which has a rainfall similar to that in Berkshire. A full study of the sources of cæsium-137 and potassium in human diet would be needed to obtain an Observed Ratio, but it appears that the discrimination factors are again much nearer unity than those observed with the strontium-90/calcium ratio.

Summary

Measurements of the cæsium-137/potassium ratio in dried milk and some corresponding results for hay have been obtained for the period 1957 and the first half of 1958. In dried milk from Driffield, which has a relatively low rainfall, the ratio in the summer of 1957 was 25–30 μμc. of cæsium-137 per gm. of potassium, and dropped to 10–15 μμc./gm. in the winter. Dried milk from Carmarthen, a high-rainfall area, showed ratios of 60–70 μμc./gm. and about 40 μμc./gm. in summer and winter respectively. The decrease in the ratio in the winter may be due to the change in feeding habits of cows, which are given supplementary food in winter. A large increase in the ratios in dried milk from all areas was observed in June 1958 and is associated with a larger than usual rate of fall-out in May 1958 and subsequent months. The average cæsium-137/potassium ratio in dried milk in μμc./gm. for the period April 1957–April 1958 is shown to be numerically equal to the average annual rainfall in inches in the area from which the milk was collected. The effect of the Windscale accident on the cæsium-137/potassium ratio in dried milk is shown to have been temporary. The cæsium-137/potassium ratio in human beings in late 1957 was about the same as that in dried milk from an area having a similar rainfall.

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RADIOACTIVITY OF SOILS, PLANT ASHES AND ANIMAL BONES

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ATTENTION has been directed by Turner, Radley and Mayneord[1] to the large variation in naturally occurring α-ray activities of foodstuffs and tissues. While at present there is little direct evidence as to biological significance, the subject is of sufficient interest to make it desirable to record some recent observations, at the Institute of Cancer Research, made possible by the kindness of Prof. W. V. Mayneord in making available to me apparatus developed for such measurements.

(1) The first observations concern the relative activities of bones of sheep, cows and of their offspring. It had been noticed from tests in New Zealand that the bones of calves and lambs were low in activity compared with those of adults, and, thanks to the co-operation of Dr. C. P. McMeekan of the Ruakura Animal Research Station, New Zealand, bones were made available by air-mail of a cow and a ewe and of their new-born offspring. The mother animals had been grazed on pasture grown on soil of α-activity 8×10^{-12} c./gm. The results are given in Table 1.

These figures indicate an activity of the bones of the offspring only 10 per cent of that of the mothers and with relatively less thorium. The capsuled samples of bone ash from the mothers have shown an increase in activity of the order of 15 per cent in the three months following equilibrium with radon, etc. These increases are under long-period observation which will be reported later. Such measurements are of interest in comparison also with similar observations on many other bones of cows and sheep and of pastures, and apart from recovery of polonium there is the possibility that mesothorium is taken up relatively more readily than radiothorium. The average activity of a large number of such bones was about 5×10^{-12} c./gm. ash (max. $1\cdot4 \times 10^{-11}$), but in the case of three Suffolk sheep, killed and dissected in 1921 by Dr. J. Hammond, the average activity as now measured was only 7×10^{-13} c./gm. ash, with 10 per cent contribution from thorium products. This smaller activity may be due to decay of mesothorium and products (half-life 6·15 years) or may possibly be due in part to lesser use of superphosphate fertilizers at that time.

Table 1. ACTIVITY OF BONE ASH (C. PER GM.)

		Total α-activity	Approximate contribution of thorium products (per cent)
Mother cow	Femur shaft	$4\cdot8 \times 10^{-12}$	50
New-born calf	Femur shaft	$5\cdot8 \times 10^{-13}$	10
New-born calf	Femur head	$5\cdot2 \times 10^{-13}$	10
Mother ewe	Femur shaft	$4\cdot8 \times 10^{-12}$	40
Mother ewe	Femur head	$4\cdot0 \times 10^{-12}$	30
Lamb	Whole femur	$4\cdot8 \times 10^{-13}$	15
Lamb	Whole tibia	$4\cdot0 \times 10^{-13}$	14

(2) The second set of observations relate to the possible influence of the superphosphate on plant and animal uptake of radioactivity. Samples of rock phosphates of various origins were collected and Table 2 gives the activity of the particular samples.

It has been suggested to me by an officer of the United Kingdom Geological Survey that the activity of fossil guano arises from fixation by the phosphate of uranium from sea spray through the ages, but the

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Table 2. TOTAL α-ACTIVITY (c./gm.)

Phosphate rock (Florida)	$2\cdot2 \times 10^{-10}$	
Ocean Island	$2\cdot1 \times 10^{-10}$	
Morocco	$2\cdot0 \times 10^{-10}$	
Nauru	$1\cdot75 \times 10^{-10}$	(*c.* 10 per cent)
Makatea	$1\cdot4 \times 10^{-10}$	
Christmas Island	$5\cdot5 \times 10^{-11}$	
Gafsa (North Africa)	$5\cdot5 \times 10^{-11}$	(40 per cent)
Peruvian phosphate (old guano)	$4\cdot5 \times 10^{-12}$	(< 10 per cent)
Peruvian phosphate (recent guano)	8×10^{-13}	

activity of Peruvian fossil guano does not fully confirm this. It is hoped to collect further samples which may provide information on this question.

It may be interesting to consider the effects on foodstuffs and animal bones of the growing use of superphosphates, a world increase of some 2½ times in the past 20 years and 10 times in the past 40 years. According to statistics from the Organization for European Economic Co-operation, approximately one million tons of superphosphate are used in the United Kingdom each year, and approximately 850,000 tons of basic slag and their content of uranium are added to the soils annually. In the United Kingdom at present, phosphate from Morocco is largely used, in New Zealand from Nauru—both active sources. This active material may be taken up by the roots into the plant or in the case of top-dressing of pastures it may, pending sufficient rainfall, remain on the leaves as dust to be consumed by grazing animals. Both these effects have been observed in the samples collected for test in the present experiments, but they were not laid out or planned with this particular type of test in view, and the quantitative aspect is influenced by varietal differences in uptake, for example, different strains of ryegrass. For plants grown in the same soil varietal differences are in general about as important as species differences, with Brazil nuts as an important exception. On average soils, plant ash shows results of the order $1\cdot6 \times 10^{-12}$ c./gm. Whole wheat and bran give results of this order also, but somewhat less and with significant varietal differences. Similarly, with the exception of such places as Devon, soils in general do not vary so much from place to place as one might expect from the activities of the parent rock material, and a general figure of 8×10^{-12} c./gm. may be used. The uptake by plants from soils is, however, governed more importantly by other factors.

Grass had been collected by the New Zealand Soil Bureau from six farms in Taranaki, New Zealand, all on andesite soil of activity approximately $3\cdot5 \times 10^{-12}$ c./gm. During the past ten years, two farms had been heavily top-dressed with superphosphate, two moderately and two received none. My measurements showed no very significant differences in activity of the grasses, especially when differing grass compositions are taken into account. More definite tests will be undertaken. In another case pasture was collected from a high-production test plot and the ash proved to have an activity of $1\cdot6 \times 10^{-11}$ c./gm. On further inquiry it was learned that the plot had been top-dressed a week or so before cutting and subsequent samples from the same plot, although at a different season, gave a value only one-tenth of this amount.

To enter into detailed description and discussion of all the results obtained would be beyond the scope of this article. Two important cases, however, are worthy of mention. The first is the soil covering of Niue Island in the Pacific. This is probably a volcanic ash shower material. Its α-activity is of the order of 7×10^{-10} c./gm., that is, some ninety times that of normal soils and with little contribution from the thorium family. By chemical analysis, kindly conducted at Woolwich, a figure of 60 p.p.m. uranium was obtained, but this would account for only about one-fifth of the activity. Qualitative α-pulse analyses conducted at Harwell indicate a major contribution of thorium-230 (ionium) and also, but less definitely, the possibility of an abnormally high uranium-235/uranium-238 ratio. If either or both of these results are corroborated, it would have very important geological significance. A study of activities of plants, bones of animals and humans of this Island will also be made shortly.

The other remarkable result is the large α-activity of slow-growing mountain pastures in Wales, Cumberland and Durham, particularly the first-mentioned. For these samples, along with many others and valuable co-operation and advice, I am indebted to Dr. Scott Russell, of the Agricultural Research Council Radiobiological Laboratory, Wantage.

At the end of the first month after ashing, the α-activity of one particular sample of Welsh grass ash was 8×10^{-11} c./gm., which rose 2½ months later to $1\cdot7 \times 10^{-10}$ c./gm. Except for the relatively small contribution of thoron as measured one might have attributed this to absorption from the soil of mesothorium and subsequent growth of radiothorium. It is hoped to secure α-pulse analysis scans of these remarkable plant ashes, also to study the uptake of uranium, radium and thorium by slow-growing plants on calcium-deficient soils and in different soil and climatic conditions. It should be noted that the last-mentioned figure of activity is greater than that of superphosphates although I am assured that no fertilizer was used.

I wish to express my appreciation to Prof. W. V. Mayneord and his staff for facilities placed at my disposal and for valuable discussion and suggestions.

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CONTAMINATION BY EXTRA-TERRESTRIAL EXPLORATION

AT the instigation of the International Council of Scientific Unions, an *ad hoc* committee was set up in April 1958 to investigate the problem of contamination by extra-terrestrial exploration. The committee consisted of: Prof. Marcel Florkin (convenor), Laboratoires de Biochimie, Université de Liège; Dr. J. Rösch, Observatoire du Pic-du-Midi, Bagnères de Bigorre, Hautes-Pyrénées (representing the International Astronomical Union); Prof. J. Bartels, Geophysikalisches Institut der Universität, Göttingen (representing the International Union of Geodesy and Geophysics); Dr. Donald J. Hughes, Brookhaven National Laboratory, N.Y. (representing the International Union of Pure and Applied Physics); Dr. P. Alexander, Chester Beatty Research Institute, Royal Cancer Hospital, Fulham Road, London (representing the International Union of Biological Sciences); Prof. W. O. Fenn, School of Medicine, University of Rochester, N.Y. (representing the International Union of Physiological Sciences); and Prof. J. Roche, Collège de France, Paris (representing the International Union of Biochemistry). Prof. P. Swings, Institut d'Astrophysique, Université de Liège, and Prof. H. C. Van de Hulst, Sterrewacht, Leyden, were present as observers. To ensure wide regional representation the convenor asked for a chemist from the U.S.S.R. to act as representative for the International Union of Pure and Applied Chemistry. Unfortunately, it proved impossible for this to be arranged.

At the second meeting of the Committee, held at The Hague during March 9–10, the following summary recommendations were passed:

The Committee on Contamination by Extra-terrestrial Exploration was established in 1958 by the International Council of Scientific Unions to meet once to find out if the problem of contamination of extra-terrestrial objects by space vehicles represents a real problem. The report of this meeting, which was held in May 1958, was that in the Committee's view there is a real possibility that early experiments might spoil subsequent research. The Committee therefore proposed to the International Council of Scientific Unions that a code of conduct be drawn up for space research with particular reference to the allocation of priorities and sequences of different experiments. The Committee stressed that such a report would require active participation by experts, especially from the field of rocket technology. The International Council of Scientific Unions accepted this recommendation, and at its general meeting in Washington in October 1958 asked the Committee on Contamination by Extra-Terrestrial Exploration to hold a second meeting. At the same time the International Council requested the National Academies of the U.S.A. and the U.S.S.R. to assist the Committee with experts in rocket technology and with prepared documents. The Committee at its second meeting held at The Hague in March 1959 was able only to start its assigned task because the complexities of the problem made it impossible for the necessary detailed technical assistance to be available.

In the interval between the first and second meetings, a Committee on Space Research has been formed by the International Council of Scientific Unions to co-ordinate world-wide space research, and this new body enjoys the support of the American and Russian Academies. The Committee on Contamination by Extra-terrestrial Exploration feels that the detailed functions proposed for its second meeting form an integral and important part of the duties of the Committee on Space Research, and at this meeting the Committee confined itself to the general formulation of the problem and review of its initial report, which has been slightly modified.

General Principles

(1) Space research offers a challenge and opportunities which should appeal to the most imaginative minds. The greatest encouragement must be given to novel and unconventional approaches, and no proposal should be sanctioned which would hamper the experimenters' freedom of action unless there are compelling reasons. On the other hand, equally imaginative thinking is required when considering possible complications which can follow a particular type of experiment. Surprises are certain, and unlikely possibilities must be borne in mind when dealing with the problem of contamination, which is better defined as the problem of reducing the risk whereby one experiment may spoil the situation for other subsequent inquiries. The question of deciding whether such a conflict is likely to arise can best be dealt with by a committee or working group engaged in planning, or advising on, scientific experiments.

(2) Ideally, scientists should be asked to inform the Committee for Space Research as early as possible of each space experiment which is envisaged and of the methods to be used in its execution. The Committee on Space Research is broadly based and contains scientists from all disciplines; it is thus able to see much more clearly than the space research specialists possible conflicts introduced by such experiments and may be able to suggest ways of overcoming these difficulties.

(3) There are a number of obvious and necessary experiments which are bound to be done, and here the Committee on Space Research working group dealing with experiments may be able to suggest priorities. While it may not be possible to avoid all types of contamination, a proper sequence can ensure that the collection of data is not thereby hindered. For example, the Committee on Contamination by Extra-terrestrial Exploration recommends positively that no 'soft' landing, which requires the release of large quantities of gases, should be made on the Moon until experiments have been successfully carried out—or at least all reasonable attempts made—to determine the nature of the Moon's atmosphere.

(4) In view of the great uncertainties which face space research, all operations which are not capable of conveying meaningful scientific data are to be discouraged even if they do not appear to carry with them a known source of contamination. Risks with the unexpected must be taken, as otherwise no space exploration is possible; but such risks must be justified by the scientific content of the experiment.

Contamination endangering Physical and Chemical Studies

(1) *The Moon's Atmosphere.* The Moon's atmosphere contains only a small amount of matter (it is estimated at less than 100 tons) and is therefore extremely vulnerable to contamination. The release on the surface of any amount of volatile material (having a molecular weight greater than 60) within this range of magnitude, such as might be given off from explosions for marking purposes or to slow down the vehicle for 'soft' landings, is likely to remain on the Moon. Another factor which a change in the lunar atmosphere might bring about is an upset in the thermal equilibrium, and careful computation will be required before the magnitude of this effect can be assessed.

The release of any chemical marker on the surface of the Moon is therefore objectionable if it involves tons of material. If it has to be done, a flare releasing material quite unlike that normally present in the lunar atmosphere should be used, so that in subsequent investigations it can be clearly recognized as a contaminant introduced by man. Both in this connexion and because of increased ease in detection, a flare produced by sodium should be considered for this purpose. The sodium *D* lines could be detected at low intensities if a monochromator is used to cut out scattered light of other wave-lengths. Probably the quantity of material required to be visible through telescope, though not to the naked eye, would be isufficient to cause serious contamination of the tmosphere.

The possibility that a flare of this type might isturb the lunar atmosphere, due to the ionization f the sodium atoms by sunlight, has been considered, ut such an effect is unlikely to persist for long eriods.

From the foregoing it is clear that detailed exploraon can very easily modify the lunar atmosphere, hich should, if at all possible, be studied spectroopically from either Earth or Moon satellites before ndings are attempted. An accidental hit by a vehicle which has failed to go into orbit would probably not be serious, since the surface of the Moon ust occasionally be subject to bombardment by avy meteorites and the possible release of trapped es by impact will not therefore cause a departure om natural conditions.

(2) *Moon dust.* The chemical composition of the dust is of the greatest interest to a wide range of sciences. Knowledge of changes of composition at different levels would also be informative, but may be difficult to interpret since bombardment by meteorites is likely to disturb the dust. For this reason mixing of some of the dust by rocket impact is unlikely to result in loss of information.

The suggestion has been made in the recent scientific literature that there are unstable structures of a high free-energy content (that is, containing a high concentration of free radicals) on the Moon, which may be caused to react explosively on coming nto contact with organic substances from the Earth. The suggestion has therefore been made that great are be taken to exclude organic substances from pace-vehicles likely to impact on the Moon. The Committee does not support the view that such a hazard exists, since such free radical structures would be triggered off by any impact which caused intimate mixing. Meteorites or solar corpuscular radiation would act as a fuse and initiate an explosive chain-reaction. The man-made object would do no more harm in this respect. The possibility that valuable information concerning cosmic dust may be lost by disturbing the surface of the Moon has been considered but is unlikely to be serious. Analysis of Moon dust can only provide a very incomplete picture of cosmic dust, because many of the constituents will be volatilized by solar radiation.

(5) *Radioactivity.* A serious danger of altering the Moon's dust will come from nuclear explosions. These will release fission products which under the conditions of extreme vacuum will enter the Moon's atmosphere and be rapidly distributed. These radioactive atoms will be in a highly reactive form and on coming into contact with Moon dust may form involatile compounds. In this way the whole surface of the Moon may acquire additional radioactivity which may interfere with subsequent radiochemical analyses that could be of the greatest value, in particular for problems relating to the history of the Moon. The explosion of a fusion device is likely to be more serious than that of a fission bomb, since the former will give rise mainly to volatile radioactive products, notably tritium, whereas the bulk of the volatile fission products are rare gases which will not combine with the Moon dust. However, the range of the small particles by which fission bomb activity is spread is likely to be very great on the Moon, and a serious danger of contamination would undoubtedly arise.

Although the relative extent of the contamination of the planets from a nuclear explosion would be very much smaller than in the case of the Moon, it may none the less be sufficient to interfere with detailed radiochemical analyses under certain conditions. Also the effect of introducing radioactivity on another planet where there may be entirely different levels of background radiation from those found on Earth could greatly influence any form of life found there. Although the objections against nuclear explosions on Mars and Venus may not be as compelling as in the case of the Moon, they are nevertheless well justified until more information is available.

Biological Contamination

Recommendation for immediate action. The sterilization of space-vehicles to prevent the spreading of spores and other terrestrial micro-organisms in the solar system is likely to present a number of technical problems that may not be easy to solve. The Committee on Contamination by Extra-terrestrial Exploration suggests that the Committee on Space Research initiates a study immediately of the methods by which the inside of space vehicles can be sterilized, bearing in mind the presence of delicate instruments that must not be damaged. As soon as possible, methods should be published by which this can be achieved, and it should be urged that all space probes be sterilized in this way. Although the Committee on Contamination by Extra-terrestrial Exploration feels that the possibility that life can persist on the Moon is sufficiently remote to justify being neglected, all Moon probes should be sterilized so that the difficult techniques of sterilization may be worked out in practice.

The outside of space-vehicles need not be sterilized, since exposure to the unfiltered solar radiation during flight will destroy all micro-organisms which have settled on the shell. The need for sterilization is only temporary. Mars and possibly Venus need to remain uncontaminated only until study by manned spaceships becomes possible.

(1) *Contamination of the Moon by living cells.* There is no reasonable possibility by which the introduction of cells such as spores or bacteria might give rise to life on the Moon of the same type (that is, containing deoxyribonucleic acid) as on Earth which might confuse later investigators. There are no cells on Earth which grow or multiply in the absence of water, and at the high vacuum of the Moon no water can exist on its surface.

(2) *Contamination of Mars and Venus.* There is a possibility of biological contamination of these planets, since there is a reasonable probability that the conditions on Mars are such that some terrestrial organisms might grow. Carbon compounds, light for photosynthesis and probably water and nitrogen are all available. It is therefore of the greatest importance that space-vehicles should not land either accidentally or deliberately on Mars (and possibly also Venus) unless all precautions have been taken to exclude living organisms from them. Otherwise the most challenging of all planetary studies, that of extra-terrestrial life, may be put in jeopardy. The same precautions in regard to the development of complex molecules which have been dealt with in respect of lunar contamination in paragraph 4 below apply equally to both Mars and Venus.

(3) *Panspermia hypothesis.* The suggestion that Moon dust might help in evaluating the hypothesis

that dissemination of life in the cosmos occurred by transport of forms of life in the cosmic dust must be rejected, because solar radiation (in a high vacuum) would decompose 'biospores' just as it decomposes cosmic dust. The possibilities by which a spore might travel through space inside meteorites involve so many improbabilities that they do not justify special consideration at this stage.

(4) *Development of complex molecules*. The basic problem concerning the origin of life is how complex molecules (on the Earth they are based on carbon) came to be built up and become replicated. It is conceivable that the interior of the Moon dust may provide some valuable clues in this direction. It is not beyond the bounds of possibility that some 'pre-life' processes may be occurring on the Moon, and these may be similar or different from those which have taken place on Earth. If there are such processes, then the introduction of 'foreign' macromo cules from the Earth may cause a serious upset in t lunar processes. Macromolecules from the Ear might under lunar conditions act as templates a provide new foci for 'pre-life' growth. If such even were started indiscriminately all over the Moon, t pattern might be distorted. It is important emphasize that living cells are not envisaged for th process, and that in this connexion a dead bacteriu from an aseptic rocket would be as harmful as a li one. The occurrence of any such growth reactio is remote and does not justify the imposition of an irksome restrictions on lunar exploration, but whe reasonably possible it should be borne in min A simple precaution against endangering futur studies might be to limit the areas of landings on th Moon and thereby to localize the effects—if any—of terrestrial templates.

OBITUARIES

Sir Owen Richardson, F.R.S.

In Sir Owen Richardson, whose death occurred on February 15, Britain lost one of her most eminent physicists.

Owen Willans Richardson was born in 1879 at Dewsbury in Yorkshire. He won scholarships, first to Batley Grammar School, thence to Trinity College, Cambridge. He was soon absorbed in research among the famous company inspired by J. J. Thomson. By the age of twenty-two, the results of his first investigations had been published, and for more than thirty years there followed a flow of papers—attacking fundamental problems of the times—at a rate which can seldom have been exceeded.

Early at the Cavendish Laboratory, Richardson carefully observed the temperature variation of the saturation electron current from a hot platinum filament (at low pressure). From considerations of kinetic theory, he quickly developed a clear explanation based on the evaporation of conduction electrons through a potential barrier at the metal surface. He obtained the formula $i = AT^{1/2}(\exp(-b/T))$, agreeing with his experiments and related formulæ, derived, apparently, about the same time by J. J. Thomson and H. A. Wilson from thermodynamical arguments. About 1903 he was elected a Fellow of Trinity College and became Clerk Maxwell Student. He was awarded the London D.Sc. in 1904.

Throughout the first fifteen or so years of Richardson's career, phenomena of thermionic emission, in the broadest sense, retained a central position in his interests; they were complicated by the inadequate vacuum and cleaning-up techniques of the times. Largely by his efforts and those of his friend, H. A. Wilson, the thermionic emission was finally formulated by $i = AT^2(\exp(-b/T))$, which is scarcely distinguishable experimentally from the original formula. Although the electron gas concept of the conduction electrons became modified, ultimately, by Fermi–Dirac statistics and wave mechanics, the second equation, Richardson's Law, remains. The early developments are described in his book, "The Emission of Electricity from Hot Bodies", first published in 1916. For his work in thermionics, a term he himself coined, he was awarded the Nobel Prize in Physics in 1928.

While still at Cambridge, Richardson's thermionic investigations led to studies of ionic recombination, of the diffusion of hydrogen through palladium and platinum and to the theory of the diffusion of dissociated gas in solution and to other projects. He had great mathematical facility.

In 1906 he was appointed to the chair of physics at Princeton University. Papers followed on the pressure shift of spectrum lines, the gyromagnetic effect, the ratio of the charge to the mass of positive ions, the energy distribution of electrons emitted by hot bodies, which, with F. C. Brown, he proved to be Maxwellian. Work followed on the reflexion of slow electrons by metal surfaces, gravitation and electron theory, theory of dispersion and residual rays, diffusion of neon through hot quartz and various projects on problems related to the work function, including the heating and cooling effects accompanying thermionic absorption and emission with H. L. Cooke, the theory of contact e.m.f., thermo-electricity and the photoelectric effect. With K. T. Compton he played a large part in the verification of the Einstein photoelectric law. He made many pioneer studies, some in collaboration with C. J. Davisson, C. Sheard and others, on the emission and properties of positive ions from heated metals and salts. He may have been the first to observe the emission of secondary electrons by positive ion impact. He also wrote on the asymmetric distribution of electrons produced by X-rays passing normally through a metal plate, etc.

In 1914 Richardson returned to England to become Wheatstone professor of physics at King's College, London. His book, "The Electron Theory of Matter", based on his Princeton lectures, was first published in the same year. It takes its place as a landmark in the history of physics. It is a model of the *ab initio*, not too contracted presentation, which university students like and deserve. Papers followed on absolute photoelectric yields with F. J. Rogers; metallic conduction, photochemical action and (1916–17) spectroscopic researches with C. B. Bazzoni. Limiting frequencies in the spectra of hydrogen and helium for 800-V. electrons were observed at 950–830 A. and 470–420 A. and compared with Bohr's calculations. Further theoretical work on the gyromagnetic ratio followed. In 1924 he was appointed Yarrow research professor of the Royal Society, thereby being relieved of teaching duties. He began extensive investigations of the spectrum of molecular hydrogen with T. Tanaka, K. Das, P. M. Davidson, T. B. Rymer and others, and he himself made major contributions to the analysis of this most difficult of all molecular spectra. His book, "Molecular Hydrogen and its Spectrum", published in 1934, was based on his Silliman Memorial Lectures at Yale University. He retained interest in the H_2 triplet fine structures, on which he had unpublished high-resolution data, almost up to the time of his death. His last paper appeared in 1953; he had retired from the Yarrow professorship in 1944. Other work at King's College included an attempt, very early in the era of wave mechanics, to calculate the cold emission from metals under intense fields, and, in collaboration with H. T. Flint, interesting speculation concerning a least proper time.

Soft X-ray spectra of several metals were studied, especially with the late F. C. and Mrs. Chalklin. Extensive investigations of the emission of electrons during chemical reactions were undertaken, first with the late L. G. Grimmett and later with A. K. Denisoff. He acquired a splendid reflexion echelon for measurement of the wave-numbers and structure of the Lyman α line of H. He collaborated with W. E. Williams and J. Drinkwater in first measuring the wave-numbers and structures of the $H\alpha$ and $D\alpha$ lines to test the Dirac theory. Regrettably, a mysterious error crept into these observations. The results misled physicists until the Lamb–Retherford experiments. He made a notable study (1944) with the late Irena Gimpel of the reflexion of very slow electrons by copper, with apparatus earlier perfected by A. M. Crooker.

Richardson received honorary degrees of the University of Leeds (D.Sc.), St. Andrews and London (LL.D.); he was an honorary Fellow of King's College, London, and Trinity College, Cambridge. He was knighted in 1939. He was president of the Physical Society during 1926–28 and its honorary foreign secretary during 1928–45, which capacity included entertaining many distinguished foreign visitors.

There will be many who will recall his generous hospitality, and his first wife, the sister of H. A. Wilson, who was a most gracious hostess. He had a beautiful home with the finest English period furniture and a dazzling collection of paintings by Dutch and other old masters, fit for any national collection. About the house were several grandfather clocks, one in his library, by a contemporary of Thomas Tompion. They were wound once a week by the local clockmaker.

Sir Owen was a quiet and kindly man of few well-chosen words, but he had a keen sense of humour. He was exceedingly proud of his northern origins and could speak the Yorkshire dialect. His forebears of Dewsbury were manufacturers, in the trade of the district. One of his stories (generally true, with a good moral) concerned two of these individuals, engaged in the development of a machine for processing cloth. After much time and effort and failure in getting the machine to work, one remarked despondently to the other, "It wearnt go". After some thought, the other replied firmly, "It mun go!" The work proceeded. In due course the machine was perfected. It was called the Mungo machine.

Richardson was versed in botany and nearly took up this subject at Cambridge instead of physics. He kept a fine garden. About the outbreak of the Second World War he bought a large farm, some miles from his home at Alton, Hampshire, and supervised this for several years. He bought it as an investment, as a war effort, and, he said, to try and get back the fortune lost there by some of his ancestors who had migrated south to that part.

His two sons and a daughter and his second wife survive him. His elder son is professor of physics at Bedford College, London. E. W. Foster

Dr. W. H. Mills, F.R.S.

The sudden death of William Hobson Mills on February 22, at the age of eighty-five, deprived Cambridge chemistry of its last link with the nineteenth century. Mills went up to Jesus College from Uppingham in 1892, and took first classes in both parts of the Natural Sciences Tripos. After his election to a research fellowship in 1899, he went to Tübingen to work with von Pechmann, and there began his life-long friendship with N. V. Sidgwick. Upon his return to England he left Cambridge to become head of the Chemistry Department at the Northern Polytechnic in London, and during his ten years there he began the stereochemical work which was to gain for him an international reputation. He returned to Cambridge in 1912 as a Fellow of Jesus and demonstrator to the Jacksonian professor (then Sir James Dewar), and he remained there until his death.

Mills's achievements in the field of stereochemistry will always rank among the most powerful contributions made to the subject, for he had a flair for planning and carrying out a decisive experiment. By the synthesis and resolution into optically active forms of suitable compounds, he and his colleagues successfully demonstrated the non-linearity of carbon, nitrogen and oxygen in the oximes, the tetrahedral distribution of valencies in substituted ammonium ions and zinc complexes, and the planar configuration around 4-co-ordinated dipositive palladium and platinum. He played a great part in developing the steric theory to account for the optical activity of certain ortho-substituted diphenyls, and he later extended the idea of steric hindrance to free rotation to naphthalene, quinoline and benzene derivatives. Mills and Maitland, by their demonstration of optical activity in 1 : 3-diphenyl 1 : 3-di-α-naphthylallene, confirmed a prediction made fifty years earlier by van't Hoff and, as a writer in the "Annual Reports on the Progress of Chemistry" put it, "realized one of the ambitions of all stereochemists". Mills also made important discoveries in connexion with the chemistry of cyanine dyes and alkyl-substituted pyridines and quinolines.

Mills was elected to the Royal Society in 1923, and he received the Davy Medal in 1935; he was appointed to a personal readership in stereochemistry at Cambridge in 1931, and he was George Fisher Baker Lecturer at Cornell in 1937. Unfortunately, he could never be persuaded to publish the lectures and, indeed, throughout his life he seldom published anything but self-contained original papers. He was president of the Chemical Society during 1941–44. After his retirement, he seldom visited the laboratory, but he retained a wide interest in scientific matters, and his 1942 Pedler Lecture on "The Basis of Stereochemistry" anticipated much that has since been written on that subject.

No account of Mills's life would be complete without a reference to his extensive knowledge of the British flora and ornithology. He also had a long memory and a good knowledge of Cambridge history, and his excellence as a *raconteur* made him always entertaining company in the combination room of the College of which he was for nearly fifty years a Fellow, and during 1940–48 President. A. G. SHARPE

The Rev. H. H. Symonds

THE Rev. H. H. Symonds died on December 28, after a long and painful illness; by his death, the Council for the Preservation of Rural England, the corresponding body in Wales and the rural preservation movement as a whole have sustained an irreparable loss. He was a firm believer in the value and possibilities of national parks for the good of the community, and made this province especially his own. He was largely responsible for the establishment in 1935 of the Standing Committee on National Parks of the Councils for the Preservation of Rural England and Wales under the chairmanship of Mr. Norman (now Lord) Birkett. This became his absorbing interest and together with the late John Dower he took on the work of honorary drafting secretary which he carried out until 1952, when he asked to be relieved of the duties so as to enable him to devote his time to other urgent work in connexion with the North Wales (Hydro-Electricity) Protection Committee, of which he was chairman. To his labours in the field of national parks to rouse and sustain public interest may justly be ascribed the introduction of the National Parks Act and the establishment of the National Parks Commission. It was a great disappointment to him that his tenure of office as a National Parks commissioner—an appointment long overdue when it at last came—was ended so quickly and abruptly by the illness which caused his death.

Symonds was no sentimentalist. He was a very able, hard-hitting protagonist, respected by his critics and opponents and admired by his friends and supporters. He was possessed of ability and intellect of the highest order; he had the gift of making the obscure transparent and the difficult plain. We must esteem him for his unswerving fidelity to his principles and his fearless propagation of his views. It would have been a great reproach to Britain if national parks did not exist as an enduring and appropriate memorial to one who was so entirely devoted to their service. HERBERT GRIFFIN

Mr. Augustine Courtauld

MR. AUGUSTINE COURTAULD, son of Samuel Courtauld, of Courtaulds, Ltd., died after a long illness on March 3. From his Cambridge days he had been interested in exploration and had travelled in Greenland with J. M. Wordie, of St. John's College, now Sir James Wordie, and in the Sahara with Francis Rodd, later Lord Rennell of Rodd. During 1930–31 he was in Greenland as a member of Watkins's British Arctic Air Route Expedition, and during the winter manned alone the meteorological station near the centre of the ice cap. The difficulties of travel on the ice cap in the autumn had made it impossible to stock the station with sufficient food and fuel for two men, and Courtauld, at his own request, stayed there alone—a feat of personal heroism and endurance, quietly undertaken, which equals any in polar exploration.

Courtauld was not a scientist; his interests were literary, but he equipped himself as a surveyor to make himself useful on expeditions. He shared the leadership of a successful expedition in 1935 to the Watkins Mountains of East Greenland. The party climbed the highest mountain in the Arctic, since named by the Danes, Gunnbjørns Fjæld, 3,700 m.

L. R. WAGER

NEWS and VIEWS

Department of Scientific and Industrial Research Wolfe Award: Dr. L. Essen, O.B.E.

DR. L. ESSEN was recently presented by Lord Hailsham, Lord President of the Council, with the Wolfe Award of the Department of Scientific and Industrial Research, in the form of a cheque for £500. This is the first of ten annual Awards to be made, under the terms of a will, to the scientist who has made an outstanding contribution to the research work of the Department during the previous twelve months.

Dr. Essen, a senior principal scientific officer at the National Physical Laboratory, received the Award for his work on the establishment of an atomic frequency standard as a basis for the future standard of time. Although the first attempts to employ molecular and atomic frequencies as 'clocks' were made in the United States, Dr. Essen was the first to appreciate the vital importance of this earlier work as a possible basis for a new physical standard of time. The cæsium frequency standard that he designed is used to calibrate the quartz clocks at the National Physical Laboratory and to monitor the *M.S.F.* standard frequency transmissions. Valuable information has been obtained on the performance of quartz clocks, the propagation of radio signals, the periodic and irregular variations of the rate of rotation of the Earth, and the value of the present international standard of time in terms of a particular frequency of the cæsium atom. The unit of time provided by the present atomic frequency standard can be determined in a few minutes to an accuracy of 2 parts in 10,000 million. This figure of merit is ten times better than that recently announced from measurements, extending over three years, of the astronomical unit based on the period of the Earth's revolution around the Sun. The National Physical Laboratory standard has, in effect, been the time standard of the world for the past three years.

Iron and Steel Institute: Medals and Prizes

THE Council of the Iron and Steel Institute has awarded the following medals and prizes: *Bessemer Gold Medal for* 1959 to Prof. Bo Kalling, until recently director of research, Stora Kopparbergs Bergslags Aktiebolag, Sweden; *Sir Robert Hadfield Medal for* 1959 to Mr. Albert Jackson, technical adviser on steelmaking to the United Steel Companies, Ltd.; *Andrew Carnegie Silver Medal for* 1958 to Dr. P. Vasudevan, Department of Metallurgy, University of Manchester, for a paper on "The Kinetics of Bainite Formation in a Plain Carbon Steel" (*J. Iron and Steel Inst.*, p. 386; December 1958); his co-authors, Dr. L. W. Graham and Dr. H. J. Axon, were not eligible for an award; *Williams Prize for* 1958 to Mr. H. C. Child, research manager, William Jessop and Sons, Ltd., for a paper on "Vacuum-melting of Steels" (*J. Iron and Steel Inst.*, p. 414; December 1958); his co-author, Mr. G. T. Harris, was not eligible for an award.

Honorary Member

Mr. Arnold Hugo Ingen-Housz, president of the Iron and Steel Institute during 1957–58, has been elected an honorary member of the Institute. Mr. Ingen-Housz, who was born at The Hague, received his technical education at the Technical University of Delft, obtaining a degree in mechanical engineering in 1911. After working with Royal Dutch Shell and the municipality of The Hague, he joined the Koninklijke Nederlandsche Hoogovens en Staalfabrieken N.V. in 1917 as technical assistant to the founder of the company, Mr. Wenckebach, in the planning and construction of the Ijmuiden plant. On the death of the founder in 1924, Mr. Ingen-Housz became joint managing director of the company, together with Mr. Kessler. When Mr. Kessler died in 1945, Mr. Ingen-Housz assumed the position of president of the management board, and held that position until his retirement this year. When he became president of the Iron and Steel Institute in 1957, Mr. Ingen-Housz was the first overseas member to receive this distinction since the late C. P. E. Schneider, who served during 1918–20.

Royal Aircraft Establishment:

Mr. S. F. Follett, C.M.G.

Mr. S. F. Follett, who has been appointed deputy director (equipment) of the Royal Aircraft Establishment, graduated with first-class honours in engineering at the University of London. He served the Electrical Research Association on switchgear research during 1924–27, and joined the Electrical Engineering Department of the Royal Aircraft Establishment in 1927, where he was concerned with the application of electrical engineering to the aeronautical field, including electric power supply systems for aircraft, engine ignition work, early application of plastics, etc. He was appointed to Ministry of Supply headquarters as assistant director of instrument research and development (electrical) in 1946. In 1950 he was made director of instrument research and development, concerned with aircraft instruments, aerial photography and bomb-sights. He was made principal director of equipment, research and development in 1954 and, two years later, deputy director general. His former responsibilities were extended to cover armament and general mechanical accessory fields. He was appointed director general, Ministry of Supply Staff, British Joint Services Mission in Washington in 1956, and held this post until he took up his present appointment as deputy director of the Royal Aircraft Establishment.

Dr. A. G. Touch

Dr. A. G. Touch has been appointed senior superintendent of the Radio Department, Royal Aircraft Establishment, in succession to Dr. J. S. McPetrie (see *Nature*, 182, 768; 1958). After graduating at Oxford, Dr. Touch served under Mr. (now Sir Robert) Watson-Watt at the Air Ministry Research Establishment, Bawdsey Manor, in 1936, where he was engaged on early work on airborne radar. In 1940, he continued the development of airborne radars at the Royal Aircraft Establishment, but left in 1941 to join the British Air Commission, Washington, until 1947. On his return in 1947 he became superintendent of the Blind Landing Experimental Unit. In 1952 he was appointed deputy director of electronics, research and development (air) at the Ministry of Supply headquarters and, in 1954, became the director responsible for the development programme for radio and radar equipment for the Naval Air Branch and the Royal Air Force. In 1956 he was appointed director of electronics research and development (ground), responsible for the development of ground radar for the Army and the Royal Air Force. At the end of 1956 Dr. Touch carried out an independent investigation into the crash of a 'Vulcan' aircraft at London Airport, at the request of the Minister of Transport and Civil Aviation. After a year (1957) at the Imperial Defence College, he returned to his previous post.

Mr. R. J. Lees

Mr. R. J. Lees has been appointed head of the Instrument and Photographic Department of the Royal Aircraft Establishment in succession to Mr. C. N. Jaques, who has taken up an appointment with the British Joint Services Mission in Washington. Mr. Lees was educated at King Edward's School, Stourbridge, and was a major scholar of St. John's College, Cambridge. He obtained first-class honours in Part I and Part II (physics) of the Natural Sciences Tripos. He also obtained a first-class external degree in physics at the University of London. Soon after the outbreak of the Second World War he joined the Air Ministry Research Establishment, Dundee, to work on radar and, apart from a period during 1955–56 when he was director of scientific research in electronics at the Ministry of Supply, London, he continued at this Establishment, now the Royal Radar Establishment, Malvern, until receiving his present appointment. For the past two years he has been head of the Airborne Radar Department of the Royal Radar Establishment.

The Nature Conservancy

In an attractive booklet in which the illustrations are liberal and sometimes coloured, the Nature Conservancy describes its growth and development since its birth ten years ago (see also pp. 917, 935 of this issue of *Nature*). Besides maps showing the location of the many nature reserves which have been established, the booklet describes the organization of the Conservancy and the way it operates under the ægis of the Privy Council. Of the staff of about two hundred employed, rather more than one-third are scientists engaged in research or conservation. The remainder include land agents, wardens and estate workers, cartographers and administrative staff. Regional officers were first appointed to different parts of England and Wales in 1953. Among the professions and skills represented by the staff are soil analysis, diagnosis of herbage eaten by voles, construction of sluices, deer stalking, mathematical design of scientific experiments, tree-planting, interpretation of aerial photographs, procedure for making by-laws, extraction of minute animals from the litter layer in woodlands, negotiations for land acquisition, control of peat erosion on high moorlands, stomach analysis of seals, use of herbicides on vegetation between high- and low-water mark, mountain rescue, recording of vegetation changes on grassland, fixation of shifting sand dunes, and interception and arrest of deer poachers operating after midnight. The booklet (obtainable from the Nature Conservancy, 19 Belgrave Square, London, S.W.1, post paid 1*s.* 6*d.*) contains details of the public relations and educational work carried out by the Conservancy and is itself a model of how such publications should be produced.

Protection of the Shropshire Hills

The Minister of Housing and Local Government, Mr. Henry Brooke, has confirmed an order made by the National Parks Commission, establishing about 300 square miles in Shropshire as an area of outstanding natural beauty. The designated area includes the fine landscape around Church Stretton, with Caer Caradoc, the Long Mynd, the Stiperstones and the long ridge of Wenlock Edge, from which it extends north-east to take in the Wrekin and the Ercall. To the south-east, parts of the Clee Hills are included, and to the south-west the Clun Forest area on the Welsh border. Responsibility for preserving and enhancing the natural beauty of the landscape rests with the local planning authority, Salop County Council. Government grants can be made at the rate of 75 per cent toward the cost of treating derelict land, tree planting and preservation work. Grants are also available toward expenditure incurred in making agreements or orders for public access to open country and in appointing wardens. Designation does not of itself provide any additional right of access to private land.

Chinese Scientific Literature

The Lending Library Unit of the Department of Scientific and Industrial Research has started to collect Chinese scientific literature, and now receives regularly about 150 Chinese scientific and technical periodicals. The Lending Library Unit in London, which forms the nucleus of the new National Lending Library for Science and Technology, which will be set up at Thorp Arch, near Boston Spa, Yorks, in 1961, already has a large collection of Russian scientific literature, which is available to research, industrial and other organizations, through a loans service, and operates a scheme for the translation of Russian scientific literature, in collaboration with the U.S. National Science Foundation. This may possibly be extended in the future to include scientific literature from China.

Bulk Production of Silicon in Britain

Imperial Chemical Industries, Ltd., has brought into operation a large-scale development plant for the manufacture of high-quality silicon of semi-conductor grade. This remarkable material, which costs more than £100 per pound, has become of commercial importance during the past few years in the manufacture of semi-conductor devices, such as transistors, which are fast replacing conventional thermionic valves in many applications. The I.C.I. plant is operated by its General Chemicals Division on Merseyside. By the middle of this year capacity will approach 4,000 lb. per annum. Plans for much larger production are well advanced. Lump silicon, *p*-type, of resistivity greater than 200 ohm cm. is now available in quantity. Silicon in rod form, deposited direct from vapour and of exceptionally low boron content, is being produced in limited quantities in lengths of 24 in. and diameters up to 1 in. These rods are suitable for zone refining.

Smoking Habits

It often happens that investigators, particularly in the social sciences, must try to collect the information which they need by using questionnaires. One of the many problems that are apt to arise concerns the reliability of answers to questions which require an exercise of detailed and specific memory. Recently, the Tobacco Manufacturers Standing Committee issued a Research Paper (No. 2) entitled "The Reliability of Statements about Smoking Habits", by G. F. Todd and J. T. Laws (pp. 50; 1958). This should be consulted by anybody who has to try by questions to obtain factual information about habits or events covering any period in the past from a month or two to several years.

The authors show how statements about current smoking habits are generally reconstructed from a sort of 'mental picture' that the informant has of himself 'in his role as a smoker'. Changes in smoking habits are far more frequent than is generally thought to be the case, and so any information about them which refers to the past, based, as it must be, upon a general and personal assessment of current practices, is very likely to be in error. But the changes do not appear to be distributed in a random manner and, provided the sample groups investigated are large enough and the questions asked are answered seriously, so far as group tobacco consumption is concerned, information gained in this way is probably reasonably accurate in a statistical sense. For individuals, recall is frequently mistaken both as regards the amount and the kind of smoking carried on. Apart from the special topical interest of this study, it has wide methodological implications which ought to be considered by all users of questionnaires.

Bibliographies on Geology

Within recent years the United States Geological Survey has been very active in the publication of annotated bibliographies ranging over a wide spread of geological topics, many of them of world-wide interest. Among these works is a series of "Contributions to the Bibliography of Mineral Resources" (*Bulletin United States Geological Survey*, 1019*A-L*; 1954–58), which embrace separately published chapters reviewing the literature on the iron-ore resources of the world, on the world's quicksilver, titanium and nickel ores, and on the domestic distribution of magnesium salts, thorium and rare-earth deposits, salt beds, asbestos, and various industrial rocks. A second series of "Selected Bibliographies of Uranium Geology" (*Bulletin*, 1059 *A-E*; 1957–58) reviews the principal papers on uraniferous coal deposits, phosphorites, hydrocarbons, and uranium-bearing sandstones and igneous rocks in North America. Similar reviews of the international literature (including Russian works) on geophysics are published quarterly under the title "Geophysical Abstracts" (*Bulletin*, 1048, 1956; 1066, 1957; 1084, 1958); and another noteworthy compilation in the same category is "Bibliography of North American Geology", published yearly. A recently published bibliographical index to North American geology for the decade 1940–49 extends to 2,200 pages (*Bulletin*, 1049, 1957).

Apart from *Mineralogical Abstracts* (shortly to be published in a new format), British activity in geological bibliography has not of late been noteworthy, and for twenty years the only literature list covering Great Britain has been one compiled in the Library of the United States Geological Survey and published by the Geological Society of America. At the British Commonwealth Scientific Official Conference on Geology and Mineral Resources in 1948, it was resolved that each Geological Survey should produce an annual volume of abstracts covering its home ground. Most Commonwealth countries have now fulfilled this obligation, but there is not yet available any systematic compilation of abstracts covering the 300 or so papers on the geology of Britain published each year. In current international conversations on abstract journals in geology, it is to be hoped that this British domestic responsibility will not be overlooked.

Time Measurement

It will come as a surprise to many people who take their modern time services for granted to read that the first mechanical clock was made in the fourteenth century and that in earlier times the sundial and water-clock were the chief time-keepers. The Science Museum, South Kensington, has recently published the fourth edition of Part 1 of its Handbook of the Collection illustrating Time Measurement (pp. 60 + 12 plates. London: H.M. Stationery Office, 1958. 5*s.* 6*d.* net). Compiled by Dr. F. A. B. Ward, it traces the history of time measurement from its beginnings through the development of mechanical clocks and watches to chronometers. Chapters are devoted to electric clocks, including the Shortt free-pendulum and the synchronous motor clocks, to the quartz-crystal clock and to the atomic clock. Two chapters on chronographs and on various accessory mechanisms conclude the Handbook. Three hundred years ago, when the first pendulum clock was developed by Huygens, the maximum accuracy attainable was an error of ten seconds a day. To-day, the cæsium atomic clock has an error not exceeding one second in three hundred years, an improvement compared with Huygens's clock by a factor of one million. Indeed, the measurement of time is the most precise measurement of any physical quantity yet attained. This high accuracy is far beyond that required for civil purposes, and astronomers and geophysicists are likely to derive the most important benefits from the extreme accuracy now available. Those who are less interested in modern developments than in the history of science will welcome this descriptive Handbook for its account of the mechanical and electrical inventions which have contributed to the improvement of time-keeping.

Basic Biodynamics

In a recent publication, E. J. Kempf (*Ann. N.Y. Acad. Sci.*, 73 (4), 871; 1958) discusses current ideas on the interplay of genes and cytoplasm in relation to tissue and organ differentiation of multicellular organisms. After pointing out defects in existing explanations, he postulates six basic laws of biodynamics which he believes will "provide the biological sciences of genetics, cytology, embryology, biochemistry, physiology, psychology and sociology with a formulation of the basic natural processes involved in their special fields of investigation. These laws will clarify and facilitate the further development of secondary laws of the sciences of living behaviour". This somewhat extravagant claim is put forward in a singularly obscure and cumbersome style. Nevertheless, the paper contains a number of novel and stimulating ideas, and is worth close study.

Instruments in Industry

Evans Electroselenium, Ltd., Colchester Road, Halstead, Essex, has issued a series of twenty leaflets, each applicable to a particular industry, entitled "Instruments in Industry", which form a comprehensive guide to the various determinations that can most usefully be carried out using EEL photoelectric instruments. The fields of application include agriculture, ceramics, food, glass-making, medicine, photography and printing, plastics, sewage and water analysis, and textiles. The company has also produced a series of detailed method sheets for use with the EEL absorptiometer, the EEL flame photometer and the EEL colorimeter.

Textile Institute Scholarships

The Textile Institute is offering the following scholarships, for which applications should be made before April 30. The Textile Institute Cotton Industry War Memorial Trust Scholarship is intended to enable the holder to follow a whole-time course of study in textile technology at an advanced level (preferably, though not necessarily, a degree course) and/or obtain industrial training and experience of a special character at home or abroad for a period of three years. It has a maximum value of £300 for each of the first two years and £350 for the final year. The Peter Coats Scholarship is for two or three years to a value of not more than £100 per annum, for students at present studying in a public, grammar, or secondary technical school, or attending a part-time course at a technical college, who wish to take a course leading to a college diploma or other qualification in subjects connected with the cotton industry. The Rowland Spencer Scholarship, established in memory of the late Rowland Spencer of Helmshore, Haslingden, Lancashire, is open annually for training or research, to young persons of British nationality by birth who intend to enter and make their career in the textile industry and who are in their last year at a public, grammar, or secondary technical school or attending a technical college, or who have already qualified in textile technology, either as university graduates or as associate members of the Textile Institute. There is an annual grant of £100 during the period of this scholarship.

Canadian Society of Plant Physiologists

The Canadian Society of Plant Physiologists was founded at a meeting held in Saskatoon, Saskatchewan, on October 27, 1958. The new society grew out of a series of annual research conferences on plant physiology that had been held at various Canadian universities and research institutions during a period of eight years. The officers of the new Society are: *President*, Paul R. Gorham; *Vice-President*, E. R. Waygood; *Secretary-Treasurer*, D. Siminovitch; *Eastern Director*, R. O. Bibbey; *Western Director*, Stewart A. Brown. Correspondence can be addressed to the Secretary-Treasurer of the Society, Chemistry Division, Canada Department of Agriculture, Ottawa.

Biochemical Engineering

The various biological industries, including the large-scale production of citric acid, antibiotics, vitamins and other pharmaceuticals for both human and animal consumption have developed extremely rapidly during the past decade. These, together with the expanding food-processing industries, require men trained in the somewhat rare combination of fields of engineering, microbiology and biochemistry. Man has for long controlled the activities of micro-organisms and enzymes on an empirical basis, either using them for fermentation processes or inactivating them to enhance the storage life of food. A much clearer understanding of the mechanisms involved is emerging, which is bound to be applied progressively to industrial and farming problems, and which, ultimately, will do much to overcome world-wide problems of ill-health and malnutrition. Biochemical engineering will necessarily play a major part in these developments, and it is important that British universities and technical colleges provide sufficient well-trained men and women in this field, able not only to improve existing methods but also to develop new ones as the need arises. There has already been some move to provide suitable training at the University of Birmingham and elsewhere, and University College, London, is now offering a one-year postgraduate course in biochemical engineering, starting in October. It is aimed at co-ordinating fundamental chemical engineering teaching with the requirements of the biological industries and will be balanced to suit previous experience of the student.

Photoelasticity at University College, London

Fifty years ago the late Profs. E. G. Coker and L. N. G. Filon began their collaboration in the development of the photoelastic method of stress analysis. To-day the method is recognized all over the world as one of the most valuable aids to efficient engineering design. The jubilee is to be celebrated at University College London, where most of the work was carried out, by a commemoration lecture and an exhibition of work in photoelasticity at the College. Sir Arnold Hall, president of the Royal Aeronautical Society, will preside at the commemoration lecture, to be delivered by Col. H. T. Jessop on April 15 at 6 p.m. The exhibition will be open on April 15, from 7 to 9 p.m., and on April 16 and 17, from 10 a.m. to 1 p.m., 2 to 5 p.m., and 6 to 9 p.m. The lecture and the exhibition will be open to the public free of charge and without ticket.

Announcements

Mr. J. McNicholas, general manager of the Manchester Rivers Department, and Dr. C. H. Mortimer, director of the Marine Station, Millport, and secretary of the Scottish Marine Biological Association, have been appointed members of the Water Pollution Research Board from April 1, in succession to Prof. J. E. Harris and Mr. A. Holroyd, whose terms of office have expired.

A one-day symposium on "Separation Processes in Analytical Chemistry" organized by the Royal Institute of Chemistry will be held in the Inorganic Chemistry Lecture Theatre, South Parks Road, Oxford, on April 24, at 10.30 a.m. There will be no charge for admission, which is not restricted to members of the Institute. Further details can be obtained from E. S. Lane, Chemistry Division, Atomic Energy Research Establishment, Harwell, Didcot, Berks.

The British Congress of Cosmetic Science, organized by the Society of Cosmetic Chemists of Great Britain, will be held in University College, Gower Street, London, W.C.1, during April 15–17. Sessions will be devoted to the analysis of raw materials; assessment of finished products; manufacturing or processing; and biological assessment. Further details can be obtained from the honorary organizer, Dr. R. H. Marriott, County Laboratories, Ltd., Honeypot Lane, Stanmore, Middlesex.

The second International Conference on Operational Research organized by the International Federation of Operational Research Societies (IFORS) will be held in Aix-en-Provence, France, during September 5–10, 1960. Suggestions for papers should be sent to the Secretary of IFORS, 11 Park Lane, London, W.1, before May 1, 1959, with a copy to the Secretary of the Operational Research Society of the country of origin. Manuscripts will be required by December 1, 1959, so that preprints can be made available before the Conference.

A symposium, intended for health physicists of atomic energy centres or installations, is being organized by the European Nuclear Energy Agency and the Danish Atomic Energy Commission, in co-operation with a number of scientists from Europe, from the United States and from Canada. It will be held at the Danish Atomic Energy Commission research centre at Risø, near Copenhagen, during May 25–28. The purpose of the symposium is to discuss scientific and technical aspects of health physics in atomic installations (radiation protection, control of radioactive contamination, emergency measures). Further information can be obtained from the European Nuclear Energy Agency, 38 Boulevard Suchet, Paris 16.

The twenty-fourth Cold Spring Harbor Symposium on Quantitative Biology will be held during June 3–10. The topic of the meetings will be "Genetics and 20th Century Mendelism"; and geneticists, anthropologists and palæontologists will participate. Individual sessions will deal with the theory of the gene and raw materials of evolution, natural selection and race formation, ecological systems and social organization, isolating mechanisms and speciation, the fossil record and rates of evolution, and trends of evolution. The Symposium is open to all who are interested, but because of limitations of space it is important to make advance reservations. Further information can be obtained from the Biological Laboratory, Cold Spring Harbor, New York.

The Tenth Congress of the International Astronautical Federation is to be held at Church House, Westminster, during August 31–September 5. Papers will not be restricted to a single theme, but will cover a wide range of astronautical topics, including: research applications of satellites and space-probes; existing and proposed projects for manned and unmanned space vehicles; conventional and unconventional methods of propulsion in space; problems in dynamics, control and navigation; re-entry problems; biological and medical aspects of manned spaceflight; legal problems. Papers for presentation should be submitted by June 1. Further details can be obtained from the Congress Secretariat, British Interplanetary Society, 12 Bessborough Gardens, London, S.W.1.

Nutritional Biochemicals Corp. of Cleveland, Ohio, has recently published its new catalogue listing more than 2,500 biochemicals for use in research and industry and now available through the Cleveland company. The catalogue can be obtained from the Nutritional Biochemicals Corp., 21010 Miles Avenue, Cleveland 28, Ohio.

THE NATURE CONSERVANCY

REPORT FOR 1957–58

THE ninth annual report of the Nature Conservancy for the year ended September 30, 1958*, follows the pattern of the previous report. There is a brief reference to the examination of the Conservancy's work conducted by the Select Committee on Estimates, and the Committee's recommendations in its seventh report for the session 1957–58 are being carefully studied. The declaration of fourteen new reserves during the year brought the total in Great Britain to seventy, with an area of 133,081 acres, and better progress was made in overtaking the arrears of estate management on existing reserves and in the preparation of management plans. The principles of land use and management emerging from ecological research and conservation have begun to take shape and to secure wider recognition, as in the recent reports of the Royal Commission on Common Land and of the Committee of Inquiry into Inland Waterways, and in the Government's introduction of a Bill for the conservation and control of red deer in Scotland on the lines of the recommendations submitted by the Nature Conservancy and the main interested national organizations in Scotland.

Research grants to universities and outside bodies were again severely restricted by lack of funds, but the Conservancy welcomes the review of grant policy described in the last annual report of the Advisory Council on Scientific Policy and is examining its own functions in this respect. Three new grants became effective during the year and eight were extended or renewed. The creation of the new Council for Nature is warmly welcomed, and the Conservancy is already planning liaison with the Council in the fields of education and public relations.

The recommendations of the Royal Commission on Common Land regarding the avoidance of permanent enclosure and the preservation of common land as a national reserve to be available for multiple uses are closely in line with the Nature Conservancy's approach, but the Conservancy considers that the absence of detailed provisions for enabling commons in poorer areas to be brought under satisfactory management in the national interest, or in that of adjoining wealthier regions wishing to use common land for amenity or other purposes, is a serious weakness, and the report appears to pass somewhat lightly over the very real problems of relating the use of each area to its soil capability and to the use of adjoining areas of common land.

The Nature Conservancy considers that the findings and recommendations of the committee of inquiry into inland waterways deal adequately with matters raised in the Conservancy's evidence to the committee. No evidence was submitted by the Conservancy on the future of the Norfolk Broads, and while the committee was not impressed by the proposal to make the Broads a national park, it thought that an expenditure of £30,000–£60,000 a year in place of the present £19,000 would be sufficient if the Great Yarmouth Port and Haven Commissioners were reconstituted (possibly including nominees of the National Parks Commission and the Nature Conservancy). The Conservancy agrees that these proposals would not run contrary to the interests of the naturalist and scientist, as some broads are unlikely to be restored to navigation and can be retained primarily as nature reserves. Moreover, the Conservancy urges that it is imperative to stay the deterioration of the broads and that this would not prejudice further action in the light of long-term research. The Conservancy considers there is no reason why agreement should not be reached on these lines.

Apart from recording progress in national nature reserves, the section of the report dealing with conservation is of particular interest for the details given of the management plans for three reserves: Woodwalton Fen (Huntingdonshire), Roudsea Wood (Lancashire) and Newborough Warren–Ynys Llanddwyn (Anglesey). For the first the objectives are: to conserve the characteristic plant and animal communities, including rare species of special interest which exist on the Fen; to encourage and carry out research and survey work on the fauna and flora of the Fen, and any other subject which may increase our knowledge of fen natural history and the factors which influence it; and to permit access to the reserve by interested members of the public, provided a permit is held, and to allow reasonable collecting, as well as to maintain good relations with neighbours with respect to boundary dykes, water levels in external systems and control of pests. For Roudsea Wood, the plan aims to establish a sample of native woodland characteristics of north-west England; to encourage the fauna and flora associated with this; and to provide facilities for study and research. The principal objectives at Newborough Warren are to carry out detailed surveys and to compile records of the entire range of scientific interests; to conserve examples of distinctive dune and slack flora and fauna; to increase the diversity of wild life within the reserve by extending some habitats and creating new ones; to enrich the ornithological interest, by influencing the balance of populations to preserve adequate numbers of species of birds and mammals most characteristic of the habitat; to control public access by a permit system, but to allow as much freedom as is compatible with conservation and research; and to develop the educational potentialities of the reserve.

Both the sections of the report dealing with conservation and that dealing with scientific research describe in some detail the rapid progress made in providing man-power, accommodation and other resources to make a firm base for research and con-

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* Report of the Nature Conservancy for the year ended 30th September, 1958. Pp. vi+119+14 plates. (London: H.M. Stationery Office, 1958.) 6*s.* 6*d.* net.

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servation on the Isle of Rhum. It has been shown conclusively that it is impracticable to produce commercial timber on Rhum, and the immediate and medium term productive potential of Rhum is being assessed, particularly as regards livestock and red deer. The Macaulay Institute of Soil Research is making a comprehensive soil survey, and a preliminary report has already resulted on the soils and geology of Rhum. A programme of vegetation recording has presented a picture of widespread erosion of the soil and deterioration in the quality of the cover.

In this report the section describing the scientific advisory services of the Conservancy is specially interesting. At Milford Haven the developers submitted new alternative proposals involving the exploitation of old gravel workings high up the shore, which will not be inimical to the scientific interest of the area, after it had been pointed out that the original plan to extract sand and gravel from Dale Bay and the adjacent Gann Flats would destroy the existing delicate balance of environment and living organisms within the Crabhall Saltings and the Dale Bay shore. The outcome of this case thus illustrates how early and full discussion between developers, planning authorities and the Conservancy can avoid developments which would be inimical to wild life. A detailed biological survey of the estuary is being undertaken by Prof. E. W. Knight-Jones with a grant from the Development Commission. Increased urgency was expressed over the conservation and use of water and the need of ancillary research, particularly in opposing the Tees Valley Water Board's proposal to build a reservoir in Upper Teesdale, and special attention has been directed to accurate methods of measuring rainfall, loss of water from evaporation and run-off.

Further representations were made in connexion with the use of chemical sprays to control vegetation on roadside verges, but it has not yet been possible to set up the panel on risks to wild life. The Conservancy has not so far received any substantial evidence that toxic chemicals used in agriculture are causing any important or widespread reduction in bird or mammal populations. The red deer survey undertaken by Dr. Fraser Darling has now provided detailed information on about one-third of the ground in Scotland on which red deer are established, and sufficient material to prepare, negotiate and adopt a soundly based national scheme for red deer conservation and control in Scotland acceptable to all the main interests concerned. The Conservancy has been enabled to develop a red deer research programme and provided with the experience and resources to undertake further development of investigation and advising services in this field. The present red deer population of Scotland is estimated at about 120,000, and it is hoped that the Deer (Scotland) Bill, which received its second reading in the House of Commons on February 3, will put a stop to the cruelty from poaching by gangs, which is the most urgent aspect of the problem. The red grouse investigation continued, as well as research on seals on the Farne Islands. The Development Commission was considering the possibility of a grant to continue and expand the research on grey seals by appointing a zoologist to investigate the fishery and marine biological aspects.

Among the research programmes which have already yielded definite results is the vegetation survey of the Scottish Highlands which had led to improved understanding of the reasons for the striking patterns of contrasting heather and grass moorlands and bracken and scrub-covered slopes which are so conspicuous in the Highlands. The Conservancy proposes to apply this knowledge within its own mountain reserves and to attempt to unravel some of the problems the Survey has indicated with the view of demonstrating a sound system of hill management. The geological survey of the Moor House Nature Reserve has been in progress for four years and work continued on the experimental introduction of Arctic–Alpine and montane species of plants into selected areas fenced off to exclude sheep. A study of the productivity of alluvial grasslands was initiated as well as longer-term experiments to estimate the annual production of plant material by peat under different regimes of extraction cropping. Other experiments at Moor House relate to the reclamation of eroded peat areas, the establishment of high-level woodland, the relation between seasonal growth in height of Scots pine, rowan and birch, and air temperature and soil temperature at rooting depth. In a further study of the craneflies (Tipulidae) particular attention is being paid to the short-palped craneflies which are restricted to peat moor.

In Snowdonia investigations on the soils, vegetation and land use continued, and the recording of chalkland grassland transects in south-east England has afforded evidence of continued increase in the proportion of the more palatable grasses and the legumes in places where the numbers of rabbits had been much reduced.

Seven important papers have now been published on the development of woodland conditions under different trees and major sections of this research are now complete. In the present report, work on the influence of site factors on sessile oak (*Quercus petraea*), Scots pine (*Pinus sylvestris*) and silver birch (*Betula verrucosa*) is described, as well as continued studies on the oak and ashwoods of northern England, and on the defoliation of oaks by the oak-leaf roller moth (*Tortrix viridana*). Besides detailed studies of the ecology of earthworms at the Moor House Nature Reserve, the study of earthworms in woodland soils is an expanding part of the work of the Merlewood Research Station. Studies of the ant populations of east Dorset heathland and on dragonflies continued, as well as the study of the population cycle and food of the short-tailed vole (*Microtus agrestis*), and the investigation on the pine martin on Benin Eighe. In coastal research the survey of brackish marsh communities of *Spartina townsendii* in Poole Harbour was extended from Arne Bay to the north shore of the harbour at Keyworth and Lytchett Bay. Studies are being made of the rate of accretion of mud on *Spartina* marsh in Bridgwater Bay and of the control of *Spartina* by herbicides. A further study has confirmed that Brent geese make use of a much wider range of salt-marsh foods at Scolt Head Island than has been generally supposed. Experimental work into the movement of beach material at Bridgwater Bay has yielded interesting results on the development of shingle complexes and on the interaction of shingle and grass. The large-scale mapping of the physiographical forms of the coast eastwards of Hinkley Point has been completed. At Braunton Burrows extensive planting of marram grass (*Ammophila arenaria*) has effectively stabilized much of the dune area over which military movements had destroyed the protective cover of vegetation.

THE NATIONAL PARKS COMMISSION

REPORT FOR 1957–58

THE ninth annual report* of the National Parks Commission covers the year ended September 30, 1958, and records the establishment of three further areas of outstanding natural beauty, the Minister having confirmed the Commission's orders designating the Northumberland coast, the Surrey hills and Cannock Chase. Decisions are awaited on the Dorset coast and hinterland and the Shropshire hills, and the Commission expects during the next few months to be submitting for confirmation orders for the Cornwall areas, sections of the north and south Devon coasts, the Malvern Hills and the Sussex Downs. As regards the 'Long Distance Routes', the Commission has completed its report on the South Devon Path and its work on the North Devon Path is well advanced. Solutions are being sought for a new line in the Pennine Way, the Blakehope Fell area of Northumberland, and this will leave Edale Bridge as the only major problem of the route outstanding. The Commission again comments on the good work being done by voluntary assistance in clearing disfigurements from disused gun-sites and other sites of wartime activities in the Pembrokeshire Coast National Park, the Lake District, the Peak District and elsewhere, but rightly points out that it is a national disgrace that so many disfiguring marks should still remain. It welcomes the assurance given in the House of Commons on July 2 by the Parliamentary Secretary to the Ministry of Housing and Local Government that purchasers of an airfield are now required to leave it reasonably tidy.

As regards the National Parks themselves, the Commission's report stresses the creative work being undertaken in the Peak District, where the Board's current programme includes many plans for the removal and concealment of scars and blemishes on the landscape; public access is being extended, as well as information work and the development of the voluntary warden service. In the Lake District, caravan sites have received much attention and anti-litter work has increased, while in Snowdonia an economic survey of the Park is proposed with particular reference to amenity. Substantial agreement was also reached with the Forestry Commission, through the Forestry Consultative Panel, on the definition of zones within the Park where the Forestry Commission would undertake not to carry out planting, and of further zones where planting would only occur after consultation with the Committee. The Park Planning Committee for Dartmoor has now reached agreement with the South Western Electricity Board on detailed procedure for early informal consultation on proposals for overhead electricity supply lines within the Park, and its efforts to remove or mitigate disfigurements and advertising continued to meet with success. Anti-litter work further developed in the North York Moors, and in the Yorkshire Dales the West Riding Park Planning Committee reports further negotiations for public access to Barden Moor and Barden Fell.

The report of the Commission refers to new action to secure publicity for "The Country Code" and for national parks in general as well as to the campaign to abate the litter nuisance. Nearly four hundred development proposals were referred to it during the year, and the Commission does not conceal its disquiet at the granting of Ministerial consent for three major industrial undertakings in National Parks. These decisions must result in grievous damage to the landscape of the Snowdonia and the Pembrokeshire Coast Parks, and the particular and general issues involved are discussed in some detail in the report, while examples of other development issues handled during the year are given in appendixes. These three development proposals and a series of Acts with a direct bearing on the work of the Commission are regarded as the outstanding features of the year under review, but their implications are considered elsewhere.

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* Ninth Report of the National Parks Commission for the year ending September 30, 1958. Pp. iv+79+8 plates. (London: H.M. Sationery Office, 1958.) 5s. 6d. net.

MAGNETIC FIELD OF THE EARTH

IN recent years the maintenance of the Earth's magnetic field has generally been ascribed to dynamo interaction between the field and convective motions in the Earth's core. Such an explanation receives support from the relatively rapid fluctuations in the field and its apparent reversals during geological times. However, theoretical investigations of the suggestion have met considerable difficulties. The field is supposed to be expanded in a series of harmonics, and in order to get soluble equations it is necessary arbitrarily to chop off the series at an appropriate point. Questions of convergence arise, and though the work of Bullard and Gellman, using all the resources of an electronic computer, made the convergence appear plausible, it could do no more.

A recent paper by A. Herzenberg* has discussed a dynamo model for which the question of convergence can be decisively answered. He represents the Earth by a large solid conducting sphere; two eddies in its interior are represented by smaller solid conducting spheres with their centres some distance apart, and which are constrained to rotate uniformly around diameters. The smaller spheres are in electrical contact with the material of the larger one, in which they are imbedded.

The system operates as a self-exciting dynamo if the angular velocities of the inner spheres are sufficiently great, and their axes of rotation are suitably oriented. The mechanism of dynamo maintenance is roughly as follows. The rotation of the first sphere twists the lines of magnetic force which penetrate the sphere, and generates a magnetic field large compared with the exciting field, the lines of force of the induced field being circles around the axis of rotation. This induced field is propagated through the surrounding material to the vicinity of the second sphere, where it provides a seed field which is similarly twisted by the rotation of that sphere and provides a much larger field with lines of force around the axis of rotation. This induced field in its turn is propagated back to the first sphere, where it provides the primary field which is twisted by the rotation of the latter. With roughly half the possible directions of the axes of rotation, the dynamo interaction amplifies the existing field. Herzenberg finds it necessary to discuss the reflexion of magnetic fields at the boundary of the large sphere, but it is difficult to believe that this can have any decisive importance to maintenance of the dynamo.

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* *Philosophical Transactions of the Royal Society of London*, A, 250 (21 August, 1958): Geomagnetic Dynamos. By A. Herzenberg. Pp. 543–585. (London: Royal Society, 1958.) 13s.

Herzenberg's mechanism possesses definite advantages from the mathematical point of view. If the distance between the centres of the smaller spheres is sufficiently great, the higher-order harmonics of the field which is induced by the rotation of one sphere are strongly attenuated before they reach the other sphere. This ensures the convergence of the expansions used by Herzenberg; a large part of his paper is, in fact, concerned with the convergence. The mechanism also has the advantage that the method of feedback is clearly evident; in Bullard and Gellman's work the same mass of fluid partook of two different sorts of motion at the same time, and it was virtually impossible to separate the effects of the two motions.

Like other earlier workers, Herzenberg made no attempt to consider the reaction of the induction process on the motion which causes it, and indeed his mechanism does not lend itself to considering such a reaction. The reaction must clearly be important, and be responsible for the tendency for the Earth's magnetic axis to approximate to its axis of rotation. Thus the importance of Herzenberg's work is primarily not physical, but mathematical. It decisively clears up any lurking doubts about the dynamo theory due to defects of convergence in earlier discussions. In considering the physical picture it is now no longer necessary to worry lest deeper research may show that failures of convergence invalidate the whole dynamo hypothesis.

T. G. COWLING

RAILWAY ECONOMICS

ALTHOUGH it appeared after the House of Commons debate on December 11, when the Transport (Borrowing Powers) Bill received its second reading, the broadsheet, "Paying for the Railways" (No. 429. December 19, 1958), issued by Political and Economic Planning, throws much further light on the problem of the future of railways, reviewing briefly the origin of the financial difficulties of British Railways since the War, the policies recently proposed, including the problem of wages, and finally setting forth four possible alternative solutions. In moving the second reading of the Bill, Clause 1 of which extends the borrowing powers of the British Transport Commission by a further £600 million, the Minister of Transport and Civil Aviation, Mr. H. Watkinson, said that the crux of the problem was how the railway system of the Victorian age could streamline itself to fit the age of the motor-car and nuclear power. For the first forty-four weeks of 1958 merchandise traffic was 14 per cent below 1957 and 10 per cent on 1956. Nevertheless, the Commission was pressing on with modernization of heavy traffic, but it was inevitably slow and took long to come to fruition. By the end of 1958, fitted freight trains would represent 35 per cent of the whole and wagons fitted with continuous brakes number 270,000; 44,000 containers suitable for door-to-door carriage would be in use, 150 older marshalling yards would be closed and 27 new yards constructed. Each working day 4 million passengers and 1 million tons of freight were moved.

Mr. Watkinson said a severe fall in heavy freight traffic in the last two months of the year was the main cause of the deficit for the year, which is expected to be about £85 million. Transport of coal was at present down by about 500,000 tons a week; production of crude steel in 1958 was probably about 10 per cent lower than in 1957, and the Commission's report indicates a fall in receipts from coal and mineral transport of more than £600,000 a week on 1957, but assumes that this is a temporary decline, calling for temporary measures only.

Mr. Watkinson said that at his request the Commission had already initiated a full, detailed and urgent review of the whole modernization plan, taking account of both present and probable changes in traffic in the light of the probable level of activity in the coal industry, in view of competition from oil and future developments in nuclear energy. He hoped to lay the findings of this review before Parliament by the early spring. Meanwhile, with the Government's full support, the Commission was proceeding with more modernization on a narrower front. It proposed to concentrate resources for main-line electrification on the London Midland and Scottish line to Manchester and Liverpool and to accelerate its completion by several years. The introduction of diesel locomotives to eliminate the use of steam would be accelerated as quickly as possible on an area basis, particularly on routes north of Newcastle upon Tyne: by 1961 nearly 1,100 main line diesel locomotives would be in use. Multi-unit diesel trains would be doubled, from 2,300 to 4,600, by the end of 1961. As a result of these and other measures the Commission expected to achieve additional savings of at least £30 million in a full year. Although there had been a reduction in the labour force of 20,000 during the past year, this had been effected with proper agreements between the Commission and the trade unions. In replying on the debate, Mr. C. R. H. Nugent, Joint Parliamentary Secretary to the Ministry, referred to the encouraging position of passenger services, revenue for which in November 1958 showed an increase of £0·3 million on 1957. The Minister himself also referred to the success of some of the luxury trains and to the Commission's intention to pursue a more flexible policy in fares.

Dealing with the modernization programme, first published in 1955, the Planning broadsheet agrees that the most important feature, the gradual substitution of electric or diesel traction for steam locomotives, as well as the plans for extending automatic train control and colour light signalling, fitting all goods trains with vacuum brakes, the improvement of express train services and provision of door-to-door containers, should both provide economies and improve the quality of passenger and freight services. If the expectations of the Commission are justified, the initial cost of the modernization programme should be covered by improved revenues, and there is no justification for slowing down the programme to remove an immediate financial predicament.

The broadsheet is more critical of the policy of cutting uneconomic services, and while some adaptation of railway services is obviously necessary in the light of those provided by road hauliers and road passenger undertakings, Political and Economic Planning does not consider it is always in the interest of the railways to cut their services to solve an immediate financial problem. In reducing the frequency of passenger services the railways are following a dangerous policy of reducing costs by lowering the standard of their service, and experiment with the variety of alternative means of curtailing losses is advocated. Rejecting as economically unsound a flat subsidy without any re-organization of the national transport system, it points out that the solution of allowing the railways to operate purely as a commercial undertaking would involve a break with their long tradition of public service obligations. Although this would probably not cause serious hardship because so many alternative forms of private transport are now available, it is politically controversial although economically sound.

That also applies to the solution by joint control of the transport system as a whole by the same undertaking, as was envisaged when the British Transport Commission was created. The merits of the transport structure which emerged from nationalizing road haulage and long-distance '*C*' licence road transport, however, would depend on the way in which co-ordination plans were formulated and implemented. The solution suggested by J. R. Sargent as a solution to the problem of unremunerative public transport services depends on a compromise between a commercial undertaking and a public service with the merits of each clearly defined, and has the merit of being politically neutral on the question how far the railways should function as a public service, since the decision how many, and which, services should be subsidized is referred to another authority. It could be applied without imposing any drastic changes on the ownership of the rest of the transport sector. The choice between any of these solutions, however, involves first a Government decision whether it wishes unremunerative services to be continued. If so, the Government must decide how these services should be financed, and in choosing the method to be used, the effects on the efficiency of transport as a whole and on the current distribution of work between road and rail require careful examination. Finally, Political and Economic Planning insists that decisions on these matters are urgent.

POSSIBLE ENZYMIC MECHANISM FOR THE DEVELOPMENT OF RESISTANCE AGAINST FLUOROURACIL IN ASCITES TUMOURS

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THE uracil analogue 5-fluorouracil was introduced by Heidelberger *et al.*[1] as an antimetabolite inhibiting tumour growth. In extensive metabolic studies[2-5] it was demonstrated that the pyrimidine was incorporated into ribonucleic acid of both normal tissues and tumours and, furthermore, that the compound inhibited the incorporation of labelled formate and uracil into deoxyribonucleic acid-thymine of Ehrlich ascites cells both *in vivo* and *in vitro*. The latter finding together with similar results by Eidinoff *et al.*[6] suggested a block in the methylation of deoxyuridine-5′-phosphate. Cohen *et al.*[7] recently demonstrated such an inhibition of thymidine-5′-phosphate synthetase from *E.coli* by 5-fluorodeoxyuridine-5′-phosphate.

These studies indicate two points at which the fluoropyrimidine might interfere with nucleic acid metabolism[1,5]: (1) inhibition of synthesis of deoxyribonucleic acid through the inability of the cells to synthesize thymine; (2) formation of a 'fraudulent' ribonucleic acid containing fluorouracil in place of uracil. Both mechanisms seem to require a transformation of the fluoropyrimidine to the nucleotide stage, and such transformations to fluorouridine phosphates and fluorodeoxyuridine-5′-phosphate, respectively, were also observed to occur in the ascitic cells[3,5]. In line with this idea is also the demonstration that in several tumours 5-fluorouridine and/or 5-fluorodeoxyuridine had a considerably higher tumour-inhibiting activity than the free pyrimidine[8].

Fluorouracil also strongly inhibits uridine phosphorylase[9] and thus inhibits synthesis of ribonucleic acid from uracil. This type of inhibition might also contribute to the carcinostatic activity of the compound.

One of our laboratories has for some time been interested in the utilization of uracil for synthesis of nucleic acid as an alternative mechanism for pyrimidine synthesis[10]. It was found that the Ehrlich ascites tumour possessed relatively high activities of the enzymes uridine phosphorylase and uridine kinase which, by their combined action, transform uracil to uridine-5′-phosphate[11]:

$$\text{uracil} + \text{ribose-1-phosphate} \rightleftharpoons \text{uridine} + \text{phosphate} \qquad (1)$$

$$\text{uridine} + \text{adenosine triphosphate} \rightarrow \text{uridine-5'-phosphate} + \text{adenosine diphosphate} \qquad (2)$$

It was also found that these two enzymes occur at much higher concentrations in the tumour than in mammalian liver[12] and in most other normal tissues[13].

In the Ehrlich ascites tumour, uracil is also transformed to deoxyuridine-5′-phosphate through the combined action of deoxyuridine phosphorylase and deoxyuridine kinase:

$$\text{uracil} + \text{deoxyuridine-1-phosphate} \rightleftharpoons \text{deoxyuridine} + \text{phosphate} \qquad (3)$$

$$\text{deoxyuridine} + \text{adenosine triphosphate} \rightarrow \text{deoxyuridine-5'-phosphate} + \text{adenosine diphosphate} \qquad (4)$$

The enzymes catalysing reactions 1 and 3, respectively, have been partially separated by ammonium sulphate fractionation[14], while there is only indirect evidence that reactions 2 and 4 are catalysed by two different enzymes.

Fluorouracil can be substituted for uracil in reactions 1 and 2 and thus give rise to fluorouridine-5′-phosphate[9]. A similar substitution of uracil in reactions 3 and 4 has not yet been demonstrated, but seems very likely.

It is well known that tumour cell populations can become resistant against different types of antimetabolities when exposed to prolonged treatment. It has been suggested that such changes have a mutation-selection basis, in analogy with similar events in microbial populations[15]. Very little is known about the biochemical nature of such hypothetic mutations. The purpose of our investigation was to determine whether any change occurs in the activities of some of the enzymes described above concurrently with the development of resistance against fluorouracil. We were particularly encouraged by the report of Heidelberger *et al.*[8], who mentioned the occurrence of a line of an Ehrlich ascites tumour, resistant to fluorouracil but susceptible to fluorouridine, and also by experiments with bacterial mutants resistant against azauracil[16] and 6-mercaptopurine[17].

Fluorouracil-resistant lines were developed from the Ehrlich ascites tumour and the ascitic form of lymphoma *L* 1210 by serial transfer under prolonged treatment. Heterozygous mice were inoculated with 10^6 cells of the Ehrlich tumour while the same number of *L* 1210 cells were injected into the peritoneal cavity of *DBA*/2 mice. The animals were treated by intraperitoneal injections of 20 mgm./kgm. fluorouracil every second day, starting the day after inoculation. As a rule, 10 mice were treated while 5 were left as untreated controls. As soon as any of the treated animals developed ascites, they were punctured and about 1 ml. of fluid was collected. After appropriate cell counts have been made, 10^5 cells were inoculated to a new recipient group, consisting of 15 mice. In this new group, 10 mice were again treated while 5 served as controls. If ascites became available in the treated group, the procedure was repeated in the same way.

Three independent lines of the Ehrlich ascites tumour were treated. Considerable inhibition was obtained in the first generation, in agreement with the findings of Heidelberger *et al.*[1]. Two lines did not show any tendency to increased resistance and were lost after 3 and 5 passages, respectively. A third line showed a marked increase in resistance during prolonged treatment (Fig. 1). The increase in resistance was particularly pronounced between the third and fourth transfer, and by the fifth passage resistance was nearly complete, although not absolute, as indicated by the survival curves of Fig. 1. No additional increase in resistance has been observed during six consecutive passages under treatment.

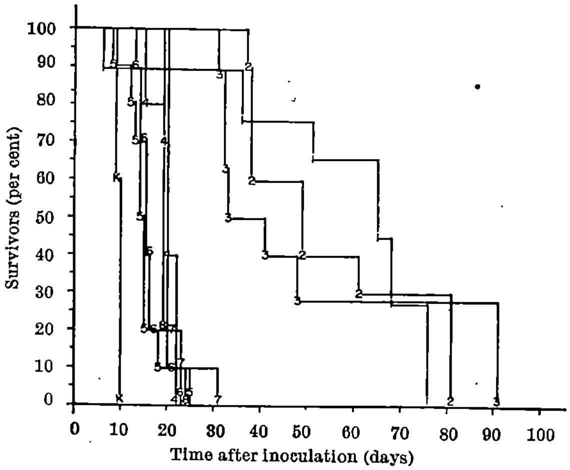

Fig. 1. Survival curves of fluorouracil-treated mice inoculated with untreated Ehrlich ascites tumour cells (group *K*) and with cells carried under prolonged treatment for 1–8 passages (groups 1–8). *K*, control; 1–8, first to eighth treated generations

L 1210 was much less sensitive than Ehrlich but showed, nevertheless, a slight but definite inhibition during fluorouracil administration. This inhibition decreased in the course of prolonged treatment and was entirely abolished after six passages (Fig. 2).

The enzymes of reactions 1–4 were assayed in extracts of acetone powder and in tumour homogenates[12,13]. Table 1 shows that, within the limits of our methods, both uridine and deoxyuridine phosphorylases were absent from the resistant Ehrlich ascites cells. Some decrease in uridine kinase activity also occurred whereas deoxyuridine kinase activity showed little changes.

In another experiment intact Ehrlich ascites cells were incubated with uracil labelled with carbon-14 at

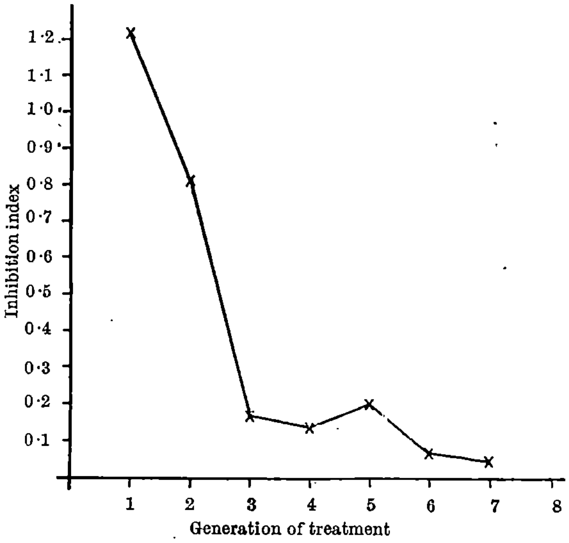

Fig. 2. Inhibition index (mean survival time of treated mice–mean survival time of controls/mean survival time of controls) of *DBA*/2 mice inoculated with lymphoma *L* 1210, under consecutive passages in the presence of fluorouracil treatment

Table 1. DETERMINATION OF ENZYME ACTIVITIES IN A NORMAL AND FLUOROURACIL-RESISTANT STRAIN OF EHRLICH ASCITES TUMOUR

	Acetone powder extracts		Homogenates	
	Normal	Resistant	Normal	Resistant
Uridine phosphorylase	74	< 0·5	11	< 0·5
Uridine kinase	80	25	5·3	2·7
Deoxyuridine phosphorylase	30	< 0·5	3·6	< 0·5
Deoxyuridine kinase	1·5	2·7	—	—

The values are given as mμmoles of product per mgm. of acetone powder or per mgm. wet weight (10 per cent homogenates) formed during 15 min. incubation at 37°.

Table 2. ANALYSIS OF ACID-SOLUBLE FRACTION FROM INTACT ASCITES CELLS AFTER INCUBATION WITH URACIL LABELLED WITH CARBON-14

	Normal cells	Resistant cells
Uracil	540	370
Uridine	1·6	—
Uridine-5′-phosphates	151	< 2
Deoxyuridine-5′-phosphate	0·8	—
Thymidine-5′-phosphates	1·5	—

The values represent mμmoles of the different compounds in one ml. of ascitic cells.

37° for 30 min. in Tyrode solution. Analysis of the acid-soluble fraction (Table 2) showed that the normal and resistant cells were permeable to uracil to about the same extent. In the normal cells uracil also gave rise to uridine-5′-phosphate. Besides small amounts of uridine, deoxyuridine-5′-phosphate and thymidine 5′-phosphates were also formed by the normal cells. No significant amounts of any of these compounds were found in the resistant tumour.

Enzyme determinations were also carried out in a normal and fluorouracil-resistant line of lymphoma *L* 1210 (Table 3). The normal tumour is much less susceptible to inhibition by fluorouracil than the Ehrlich ascites tumour, and it is interesting that in the normal lymphoma both phosphorylases show a relatively low activity. The changes in enzyme activities from the normal to the resistant lymphoma are less spectacular than in the Ehrlich ascites tumour, but it is nevertheless evident that a considerable decrease in uridine phosphorylase and kinase activities had taken place.

Table 3. DETERMINATION OF ENZYME ACTIVITIES IN ACETONE POWDER EXTRACTS OF A NORMAL AND A FLUOROURACIL-RESISTANT STRAIN OF LYMPHOMA 1210

	Normal	Resistant
Uridine phosphorylase	10	5
Uridine kinase	67	16
Deoxyuridine phosphorylase	4	4
Deoxyuridine kinase	3	3

For explanation of values see Table 1.

In summary, our experiments with the Ehrlich ascites tumour indicate that during the development of resistance the cells lost the capacity to transform uracil (and therefore also fluorouracil) to the riboside and the deoxyriboside. The fact that both enzymes are missing from the tumour might mean that the cells must lose both the ability to incorporate fluorouracil into ribonucleic acid (which proceeds via the riboside) and the ability to form fluorodeoxyuridine-5′-phosphate (which proceeds via the deoxyriboside) before a complete resistance against the drug has developed. Alternatively the loss of both enzymes might take place simultaneously through a single genetic event, even though the two enzyme activities are represented by two different proteins, which can be separated from each other by ammonium sulphate fractionation.

It is hoped that a choice between these two alternatives will be possible through an analysis of the enzyme pattern of partially resistant lines. Further experimentation is also required before one can decide whether resistance against fluorouracil in the Ehrlich ascites tumour generally is due to a lack of one or several of the enzymes necessary for the transformation of the pyrimidine to nucleotides, or whether such a mechanism only represents one of several possibilities.

This work has been supported by research grants from the Swedish Cancer Society, the Lady Tata Memorial Trust and the Damon Memorial Fund for Cancer Research. We wish to thank the Hoffmann-La Roche Co. for a generous gift of 5-fluorouracil.

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ELECTRON-MICROSCOPIC STUDY OF FINBACK WHALE MYOGLOBIN CRYSTALS

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THE visualization of the molecular arrangement in crystals of virus proteins of high molecular weight has been successfully achieved by Wyckoff and Labaw[1]. More recently, Dawson and Watson[2] studied the crystal structure of the protein ribonuclease, which has a lower molecular weight, using carbon replicas, and in addition, direct examination. These two methods of examination have also been used in the study of myoglobin described here.

The protein myoglobin has been studied in detail by X-ray analysis, and, with the information obtained, it has been possible to build up a three-dimensional model of the molecule[3]. The dimensions of the molecule are 43 A. × 35 A. × 23 A., well within the limit of resolution of the electron microscope and existing specimen preparation techniques. It would therefore seem possible that these molecules, or at least structures relating to the unit cell, could be seen in crystalline myoglobin. The dimensions of any such structures observed could then be related to the X-ray results.

The two possible approaches to the electron microscopy of protein crystals have already been mentioned. The specimen can either be examined in transmission, or by means of replicas, which give a picture of the surface topography. In the case of transmission, very thin crystals must be used to permit penetration by the electron beam. With replicas, a technique permitting the attainment of reasonably high resolution is required. Electron micrographs of the myoglobin lattice have been obtained by both methods, but the most useful information has so far come from surface replicas.

Myoglobin can be obtained from many different animals, and crystallizes in different forms[4]. In this examination, the material was obtained from the finback whale and recrystallized from sodium and potassium phosphates, the resulting crystals being known as type *F* myoglobin. The X-ray analysis has been described by Kendrew and Pauling[5]; the crystal morphology given by them is as follows.

The crystal habit is orthorhombic, the crystals being in the form of six-sided plates with the flat face the {001}. There are two inclined side faces which are {101}, and the remaining four vertical side faces are {210}, as shown in Fig. 1. It can be seen that this form of crystal is particularly suitable for electron microscopy since the {001} face will be predominant and easily recognizable, and the {210} will be distinguishable from the {101}.

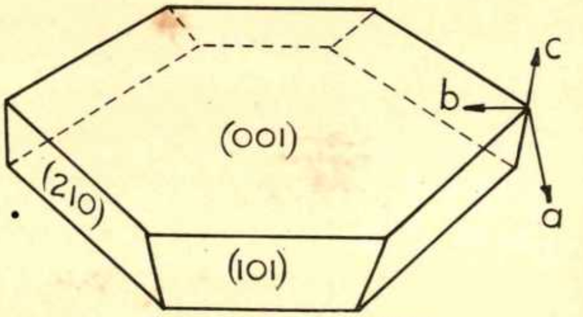

Fig. 1. Type *F* myoglobin crystal

The lattices of many proteins shrink when the crystals are removed from the suspending liquid and dried. This is the case with myoglobin; the following cell constants are given by Kendrew and Pauling[5]. In wet conditions $a = 97 \cdot 4$ A., $b = 39 \cdot 8$ A., $c = 42 \cdot 5$ A. In dry conditions $a = 88$–94 A., $b = 36$–37 A., $c = 35$–38 A. The reason why a range of values is given is that the degree of shrinkage in dry crystals is not constant.

Before proceeding with the preparation of replicas, it was necessary to separate the crystals from the ammonium phosphate solution in which they were suspended and to mount them on a suitable substrate without resuspension in any other liquid medium. This precaution was taken in order to minimize disturbance of the molecular organization. The operation was carried out by placing a drop of the suspension on a thin, freshly cleaved mica sheet which had been pierced with a needle. The underside of this sheet was pressed against a filter paper, and the suspending liquid drained through the hole, leaving the crystals behind.

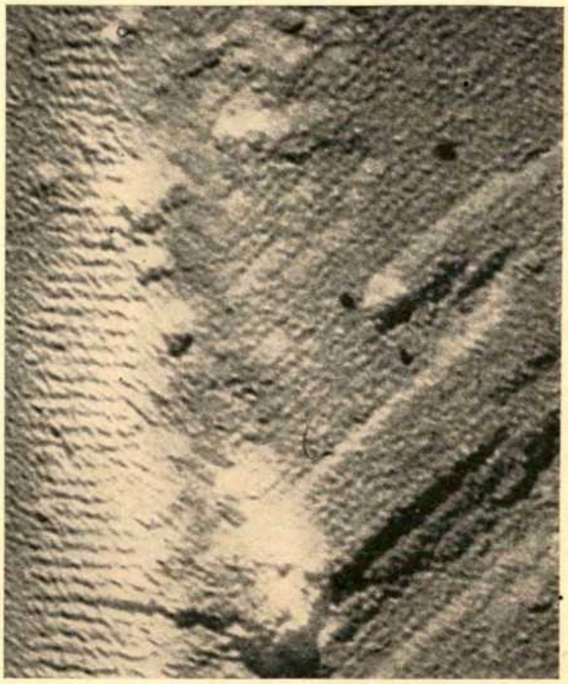

Fig. 2. {001} and {210} faces of a type *F* myoglobin crystal. Platinum/iridium/carbon replica (angle 2 : 1) The larger spacing is on the {210} face. (× 200,000)

Replicas were made by placing the mica strip in a vacuum plant and depositing a thin film containing platinum, iridium, and carbon using an evaporating technique described elsewhere[6,7]. The combined film and crystals were floated on to water, where the crystals dissolved, leaving a replica ready for mounting on support grids. The simultaneous evaporation of the three elements provided an amorphous deposit containing very sharp shadows (the angle being 2 : 1). Though the same structure could be observed using conventional platinum metal shadowing, the result was somewhat sharper using the technique described.

Electron micrographs were obtained of the three crystal faces mentioned, and of these, the {001} and {210} showed a periodic structure (Fig. 2). This consisted of dark lines parallel to the *b* and *c* axes respectively. A close examination of some micrographs indicated that the dark lines were grooves rather than steps. The spacings were measured over a number of micrographs of different crystals and gave an average value of 88·5 A. for the {001} face and 114·5 A. for the {210}. Assuming that the grooves correspond to the unit cell structure, the spacings observed on the {001} face should be equal to *a* and the spacing on the {210} to its projection, which is $\sqrt{a^2 + 4b^2}$. The value of *b* obtained by equating this expression with the observed 114·5 A. is 36·5 A. The experimental values $a = 88 \cdot 5$ A. and $b = 36 \cdot 5$ A. are consistent with the unit cell dimensions of the dry crystals.

While no periodic structures from which the value of *c* could be calculated have so far been observed, an approximate value can be estimated from the layer growth structures which have been observed on the

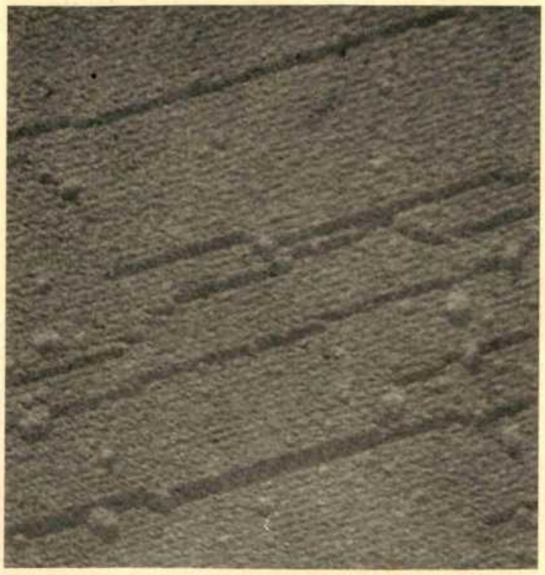

Fig. 3. {001} face of a type *F* myoglobin crystal showing layer growth. Platinum metal shadowed (angle 2 : 1) carbon replica. (× 125,000)

{001} faces (Fig. 3). The thicknesses of the layers can be calculated from lengths of shadows and should correspond to an integral number of *c* spacings. A large experimental error arises because the crystals may be tilted on the mica sheet, so giving a range of different shadowing angles. The value obtained in this way is (43 ± 15) A. Taking into account the experimental error, this result is consistent with the *c* dimension for dry crystals.

This method for measuring the c dimension is more accurate if the step consists of a large number of units (at least 10) so that the step height is large (at least 200 A.), as is the case with steps on cleaved sucrose[7].

It has already been mentioned that the myoglobin lattice can be seen in direct electron micrographs of thin regions of the crystal. This fact, together with the results of Dawson and Watson[2], indicates that it is possible to examine the lattices of easily denatured materials directly. The mechanism of image formation is similar to that proposed by Menter[8] for platinum phthalocyanine and the mineral sodium faujasite.

The results obtained here for the cell dimensions of type *F* myoglobin agree well with the results of Kendrew and Pauling. This indicates that the electron microscope can be used for providing reliable data for the evaluation of the crystal structures of materials difficult or impossible to study by X-rays.

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STRUCTURE OF SOME HYDROXIDES AND HYDROUS OXIDES

Binding of Water in some Hydroxides and Hydrous Oxides

INFRA-RED absorption spectra of hydrated aluminium oxides have recently[1] been interpreted as follows: these oxides contain hydroxyl groups, and on rehydration of the anhydrous oxides, these may be built into the lattice. In most cases no change in lattice of the oxides can be observed. The experiments were extended to compounds of the systems manganese dioxide/water[2], silicon dioxide/water and ferric oxide/water[3,4], and the presence of hydroxyl groups in these substances has been proved in the same way. We were interested in the brown precipitate formed in solutions of iron (III) salts by adding hydroxyl ions. These precipitates are either (incorrectly) formulated as $Fe(OH)_3$, or supposed to be iron (III) oxide with a very large specific surface[5]. In Fig. 1 the infra-red spectrum of a sample containing 15·1 per cent water is given, obtained from a solution of iron (III) nitrate by precipitation with ammonia, compared with the spectrum of water.

The centre of gravity of the hydroxyl band of water is located at 2·95μ. However, the centre of gravity of the band in I has moved to longer wave-lengths, between 3·1 and 3·2μ. Also an asymmetrical broadening to longer wave-lengths is observed. In I, therefore, we assume that the hydroxyl groups form O—H . . . O hydrogen bonds which are, in part, very strong because of the shorter O—H—O distance; the stronger these bonds are, the longer the OH absorption wave-length[6].

Proton magnetic resonance measurements have been carried out on aluminium and iron hydroxides and on manganese oxide hydrates (see following

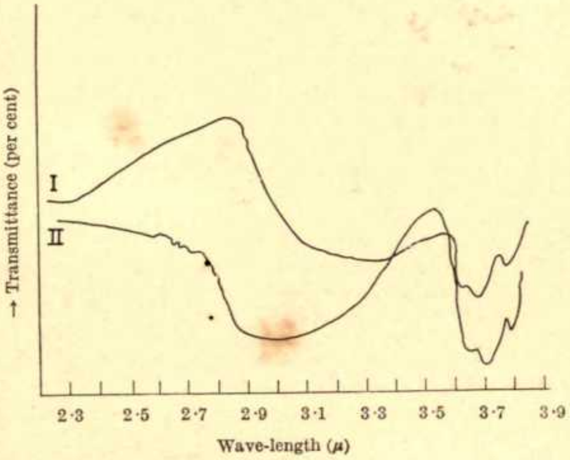

Fig. 1. Infra-red spectra (lithium fluoride prism, dispersion in 'Nujol') of iron (III) hydroxide (Fe_2O_3. 1·49 H_2O) and the spectrum of water

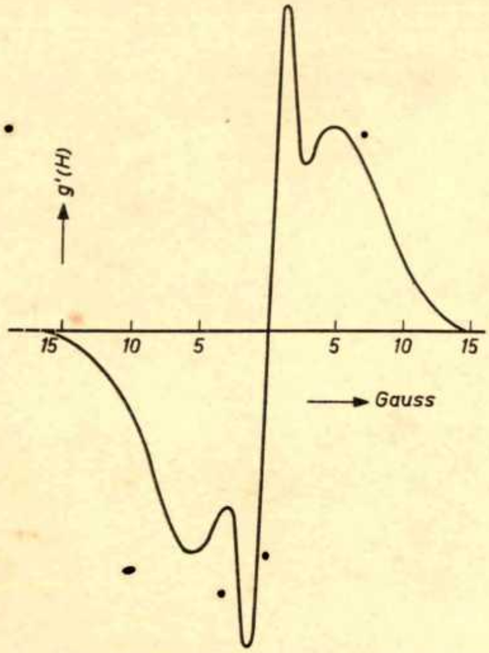

Fig. 2. Pseudo-differentiated absorption curve of boehmite (γ-AlOOH)

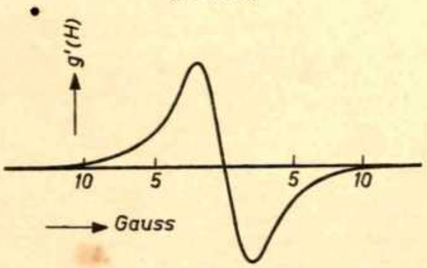

Fig. 3. Pseudo-differentiated absorption curve of an iron (III) hydroxide ($Fe_2O_3 \cdot 2{\cdot}72\ H_2O$)

communication). All aluminium oxides showed a broad line with a superimposed narrow line which is thought to be due to adsorbed water (Fig. 2). Table 1 summarizes the results for aluminium hydroxides. In general, the absorption signals of iron hydroxides and manganese oxides consist of a narrow line which is broadened at the base (Fig. 3).

Table 2 contains the results for iron (III) hydroxide gels and manganese oxides.

To obtain an absorption signal sufficiently large to permit measurement of the broad lines, it was necessary to choose a rather large field modulation (1·6 gauss). The tabulated values of the line-widths of the narrow lines are mainly determined by this modulation and are therefore too large. The tabulated percentage of adsorbed (free) water represents only a rough estimate in the cases where the narrow line and the broad base, which is thought to be due to bound water, strongly overlap.

Table 1. PROTON MAGNETIC RESONANCE RESULTS ON ALUMINIUM HYDROXIDES

Sample	Formula	Line-width (gauss)		Mole per cent 'adsorbed' water
		Narrow	Broad	
Hydrargillite	$Al_2O_3\ 3{\cdot}01\ H_2O$	2	14·3	0·8
Bayerite	$Al_2O_3\ 3{\cdot}18\ H_2O$	2·6	11·7	6
Boehmite	$Al_2O_3\ 1{\cdot}06\ H_2O$	2·6	10·5	6

Table 2. RESULTS OF MEASUREMENTS ON IRON (III) HYDROXIDE GELS AND MANGANESE OXIDE HYDRATES

Formula	X-ray data	Line-width (gauss)	Base-width (gauss)	Mole per cent 'adsorbed' water
$Fe_2O_3\ 2{\cdot}72\ H_2O$	Some broadened lines of α-Fe_2O_3	4	29	55
$Fe_2O_3\ 1{\cdot}72\ H_2O$	γ-FeOOH	4	29	40
$Fe_2O_3\ 1{\cdot}96\ H_2O$	amorphous	3·9	~33	43
$Fe_2O_3\ 1{\cdot}2\ H_2O$	amorphous	5·3	~25	25
$MnO_{1{\cdot}93}\ 0{\cdot}86\ H_2O$	δ-MnO_2	2·1	11	60
$MnO_{1{\cdot}93}\ 0{\cdot}21\ H_2O$	γ-MnO_2	2·2	25	40

Table 2, as well as the infra-red spectra, show the impossibility of isolating precipitates with the formula $Fe(OH)_3$ from solutions of iron (III) salts by the addition of hydroxyl ions. Probably the hydroxyl groups condense with the formation of water, and this may occur during aging or heating via compounds with gradually decreasing water content, until the water-free end-product, α-Fe_2O_3, is formed.

On one hand, the existence of hydroxyl groups in manganese oxide supports the suggestion of Feitknecht and Marti[7] that the deviation of the oxygen content from the ideal stoichiometric formula $MnO_{2{\cdot}00}$ arises from the replacement of oxygen ions by hydroxyl ions. On the other hand, it is difficult to consider samples with a higher hydroxyl content, for example δ-MnO_2, as polymorphic modifications of manganese dioxide.

Our results on the compounds belonging to the oxide/water system suggest two new groups of hydroxides: (1) *condensed hydroxides* resulting from the elimination of water, for example, iron (III) hydroxides, silicic acid; (2) *non-stoichiometric hydroxides* with non-stoichiometric hydroxyl contents, for example, aluminium hydroxides with different hydroxyl contents in identical lattices.

The proton magnetic resonance experiments were carried out at the Philips Research Laboratories in Eindhoven.

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Positions of Protons in Aluminium Hydroxides derived from Proton Magnetic Resonance

PROTON magnetic resonance measurements have been carried out on some aluminium hydroxides with the object of ascertaining whether the water was present in free (for example, adsorbed) or in bound form (see preceding communication). All samples consisted of powdered material. The measurements were carried out at room temperature with a simple nuclear magnetic resonance spectrometer of the autodyne type (to be published). The resonance absorption of protons was determined at a frequency of 17·5 Mc/s.

From the second moment of the absorption line $g(H)$ defined as:

$$\int_{-\infty}^{+\infty} g(H)\,(H - H_0)^2 \mathrm{d}H \Big/ \int_{-\infty}^{+\infty} g(H)\mathrm{d}H$$

information may be obtained about the positions of the protons in the crystal lattice[1]. In Table 1 the calculated values of the second moment are given, assuming a certain model as well as the second moment derived experimentally from the broad line (see preceding communication). The second moments of the aluminium oxide hydrates were calculated as follows.

Table 1. CALCULATED AND EXPERIMENTAL SECOND MOMENTS OF THE ALUMINIUM HYDROXIDES STUDIED

Sample	Second moment calculated (gauss^2)	Second moment experimental (gauss^2)
Hydrargillite	26·0	26·5 ± 1·2
Bayerite		18·8 ± 1·0
Boehmite	19·0 – 19·2	18·2 ± 1·0

Hydrargillite ($\gamma Al(OH)_3$). The structure of hydrargillite has been determined by Megaw[2]. In this structure the aluminium atoms are located between two planes of oxygen atoms which are close-packed and surround the aluminium atoms octahedrally. These planes form an *AB—BA—AB—B* . . . sequence. According to Megaw, the protons are found between these 'sandwiches'.

Fig. 1 shows the octahedron triangles formed by the oxygen atoms in one plane.

One may assume a model where the O—H bonds are directed from an oxygen atom in the lower plane to an oxygen atom in the upper plane in the next 'sandwich', but translated over one triangle side. In alternate triangles these OH bonds are pointing upward and downward (Fig. 1*a*). From this model a second moment of 26·0 gauss^2 is calculated (taking the OH distance equal to 0·96 A.). In a similar model (Fig. 1*b*), with the projections of the OH directions in the different triangles forming an angle of 120°, one obtains 29·4 gauss^2. In these models it is clear that there exists a special triangle in agreement with the X-ray data. It will be shown elsewhere that from other models a completely different value of the second moment is obtained. (For example, for the model suggested by Bernal and Megaw[3] the second moment is less than 15 gauss^2.)

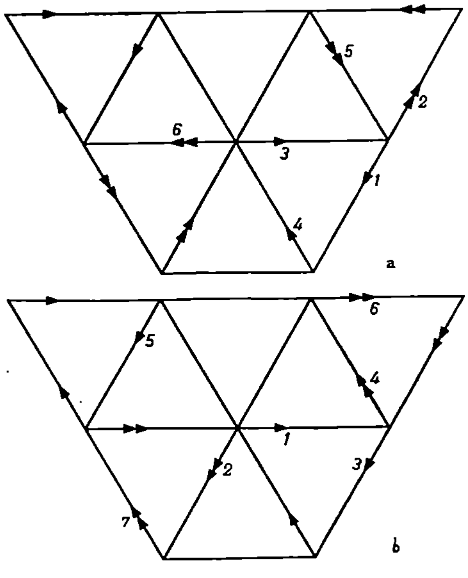

Fig. 1. Octahedron triangles of the oxygen atoms of one layer of hydrargillite: single arrows, OH bonds pointing upward; double arrows, OH bonds pointing downward

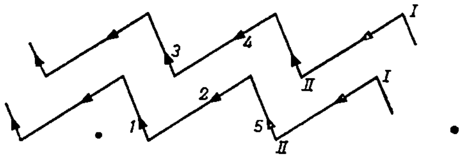

Fig. 2. Zigzag chains of the OH bonds in boehmite in the parallel position

The calculations on hydrargillite were carried out starting from a regular hexagonal structure. In practice, the octahedra are slightly deformed; the effect upon the second moment is small.

Boehmite ($\gamma AlOOH$). The structure of boehmite has been determined by Millikan and McAtee[4]. The OH directions form zigzag chains between the planes of the oxygen atoms (Fig. 2). Nakamoto, Margoshes and Rundle[5] have correlated the OH-stretching frequency and the O—H . . . O distance in different compounds. They give a graph of O—H distances against corresponding O—H . . . O distances. In this graph an O—O distance of 2·70 A. corresponds to an O—H distance equal to 0·98 A. With an assumed OH distance of 0·98 A. a second moment of 19·0 gauss^2 is obtained in the case of parallel OH bonds in successive chains, whereas for anti-parallel OH bonds one obtains 19·2 gauss^2. It is thus not possible from values of the second moment alone to distinguish between these models.

After the work described here had been completed, a recent paper of Holm *et al.*[6] came to our attention, giving experimental data and calculations of the structure of boehmite in complete agreement with our results.

Bayerite (α-$Al(OH)_3$). The structure has been determined by Yamaguchi and Sakamato[7]. They assume a model not unlike the structure of brucite, $Mg(OH)_2$, but without one-third of the metal atoms. However, the calculation of the second moment for this structure leads to values larger than 33 gauss^2. (The OH distance was assumed to be 0·98 A.)

The discrepancy between the experimental and calculated second moments is so large as to suggest a completely different structure.

We thank Prof. O. Glemser, of the Anorganisches Chemisches Institut der Universität at Göttingen, for preparing the samples.

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ACTION OF AUXINS ON *ACETABULARIA* AND THE EFFECT OF ENUCLEATION

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THE effect of auxins on algæ has never been as clear-cut as on higher plants. While some positive effects, both on multiplication of unicellular forms and on organ formation in larger algæ, have been demonstrated, many of the results have been uncertain or even conflicting. In the case of *Chlorella*, some, but not all, of the disagreement may have been due to the use of ethanol as solvent for the added auxin, since concentrations of ethanol as low as 0·01 per cent markedly increase the growth[1,2]. However, there are other sources of variation; Elliot[3] found indoleacetic acid, made up without alcohol, to promote the growth of *Euglena gracilis* at 0·1–1·0 mgm./l., while in our own (unpublished) experiments no effect could be found at any concentration with autotrophic or mixotrophic nutrition. Other factors were uncovered by Algeus[4], who has made the most thorough study to date with unicellular forms. He found indoleacetic acid (made up without alcohol) caused marked increases in cell number in two strains of *Chlorella* and in *Scenedesmus obliquus*, but not in others. There was no increase in cell size. Naphthaleneacetic acid and indole-3-butyric acid were much less effective than indoleacetic acid. He observed that the stimulation in indoleacetic acid came to an end after about six days, and traced this to photo-destruction of the auxin and consequent formation of an inhibitory product; the product of the action of hydrogen peroxide on indoleacetic acid was also inhibitory. Algeus and other workers have also reported that when sugar was added to the medium the growth is better, but the promoting effect of auxin disappeared. Presence or absence of sugar, like that of ethanol, may explain some, though not all, of the earlier discrepancies. A comparable influence of soil extract has been noted in our work reported here.

Work on the larger algæ is somewhat more definite. The growth of germinating zygotes of *Ulva*, zoospores of *Enteromorpha*, and sporelings of *Fucus* and *Ascophyllum* are all reported to be promoted by indoleacetic acid[5,6], but in the case of *Fucus* sporelings iodoacetic acid was about equally effective; the stock solutions were made up with alcohol in this case[6]. In the green alga *Rhizoclonium*, indoleacetic acid caused marked elongation, the mean cell-length being doubled at the optimal concentration, which was 10^{-9} M; the dry weight showed a smaller increase[7]. Again the stock solutions were made up in alcohol, which may vitiate these results. However, isolated apical segments of *Codium* gave a marked elongation response to 5 mgm./l. (3×10^{-5} M)[8] of indoleacetic acid, and this solution contained no alcohol. Organ formation may be promoted, too; the development of rhizoids on the thallus of *Bryopsis*[9] and *Enteromorpha*[10] was strongly promoted by indoleacetic acid, though Jacobs's method of application (suspension of a few indoleacetic acid crystals in the sea water) probably involved very high concentrations[9]. Indoleacetic acid hastened both shoot and rhizoid development on separated internodes of *Nitella*[11,12], but the action of other auxins was equivocal: naphthaleneacetic acid hastened formation of rhizoids but not that of shoots, indolebutyric acid hastened that of shoots but not that of rhizoids, while 2,4-dinitrophenol hastened neither. The effects were quite non-specific since riboflavin and ascorbic acid were about equally active; pyridoxin and niacin were also active on rhizoid formation. Another apparently non-specific effect is that of indoleacetic acid, kinetin or adenine in promoting the initiation of filaments on the thallus of *Ulva lactuca*[13]. Recently, Hustede[14] has found a striking effect of indoleacetic acid in promoting the formation of zoospores of *Vaucheria* and causing its antheridia to grow into vegetative tissue. Tryptophan has the same effect, but indolecarboxylic acid acts in the opposite direction, suppressing the formation of zoospores and promoting the formation of oogonia. Finally, Dao[15] has reported marked acceleration of growth by indoleacetic acid in *Acetabularia mediterranea*; but the effects varied with the season. Later, however, she could not confirm these results, either with indoleacetic acid or naphthaleneacetic acid, though high concentrations of the former or tryptophan still promoted growth somewhat[16]. The solutions were not changed during the experiments and became brownish due to photodestruction (cf. ref. 4). As actual growth data were not given, and the ranges of growth-rate quoted were higher for her plants growing in unsupplemented sea water than for those of other workers in the more favourable Erdschreiber solution, it is difficult to appraise this work.

The general impression from these studies is that some aspects of algal growth are indeed promoted by auxins under some conditions, but that these conditions are not well defined, the specificity of the action is uncertain and the effects are subject to wide variation. Since many processes in algæ are fundamentally the same as in higher plants, and since there is no special reason for believing that the processes of growth constitute an exception, promotion by auxin should be expected. It seemed, therefore, desirable to re-examine the problem. In the microscopic forms, cell multiplication is the only convenient criterion for growth, whereas in higher plants the most prominent effects of auxin are on cell enlargement and organ formation. For this reason an alga with large cells was preferable. The specially favourable structure and long growing period of *Acetabularia*, as well as the marked morphogenetic capacities of its parts, which have been the subject of numerous investigations, made it peculiarly well adapted for the purpose.

Plants of *Acetabularia mediterranea*, 6–9 months old and 10–30 mm. in length, were the experimental material. They were grown in Erdschreiber solution, and the experiments were carried out in artificial-light cabinets at 20° C. Erdschreiber, Schreiber solution, or sea water were used as a medium, and indoleacetic acid, naphthaleneacetic acid, or in a few cases other compounds, were used as auxins. The stock auxin solutions, from which dilutions were prepared, were made up in sea water and adjusted to pH 8·0–8·2.

Two different and independent effects of auxins on *Acetabularia* have been established in this work. They are complexly interrelated with both the simultaneous and the previous exposure of the plants to light, as well as with the nutrient solution used. In the first place, indoleacetic acid promotes elongation of the stalk. The effects range up to nearly 100 per cent increase: they can be observed in both bright and medium light, and are best seen in Schreiber's solution. The optimal concentration of indoleacetic acid is from 10^{-5} to 10^{-6} *M* (1·75–0·175 mgm./l.). An example is shown in Table 1.

Table 1. GROWTH OF INTACT *Acetabularia* PLANTS IN INDOLEACETIC ACID

Bright light, 20° C., Schreiber solution. Plants which had formed caps at 25 days omitted

Concentration of indoleacetic acid (*M*)	0	10^{-6}	10^{-5}	10^{-4}
Initial length (mm.)	19·8	20·3	19·0	19·9
Increase in next 11 days (mm.)	1·7	2·8	4·4	4·5
Increase in following 14 days (mm.)	5·2	5·0	8·7	7·2
Total increase in 25 days	6·9	7·8	13·1	11·7

In the second place, indoleacetic acid promotes the formation of the 'cap' (the organ in which the reproductive cysts are formed later). This also can be observed best in Schreiber solution, but has been noted to a lesser extent in Erdschreiber, in which all the plants, controls included, form caps more readily. The optimum concentration of indoleacetic acid for cap formation is in most experiments 10^{-4} *M*, that is, 100 times as great as for elongation. One of several comparable experiments is shown in Fig. 1.

Naphthaleneacetic acid also acts powerfully on cap formation; its optimum concentration is at 10^{-5} *M*, while 10^{-4} *M* is inhibitory and eventually toxic. It is thus clearly effective at lower concentrations than indoleacetic acid. In promoting stalk growth its optimum concentration is 10^{-5}–10^{-6} *M*, though it is apparently somewhat less potent than indoleacetic acid.

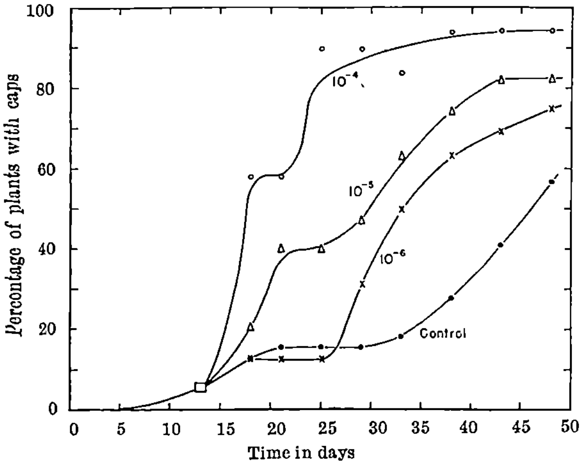

Fig. 1. Time course of cap formation in *Acetabularia mediterranea* at 20° and about 100 ft. candles white light; in Schreiber solution and with three concentrations of indoleacetic acid, 10^{-4}, 10^{-5}, 10^{-6} *M*, renewed about every 7 days

A feature of the responses, both in stalk growth and in cap formation, is that they occur only after a considerable period of time, 10 days being about the minimum for a detectable effect. Since the pH of the suspending medium is about 8·2, a value at which indoleacetic acid and naphthaleneacetic acid are fully dissociated and therefore might perhaps be restricted in their entry, a study was made of the action of the neutral auxins methyl indoleacetate and indoleacetonitrile. However, while both these substances clearly promote cap formation, and in addition the nitrile promotes elongation, their action was found to be no more rapid than that of indoleacetic acid. Indeed, the elongation caused by the nitrile was not observed at all at 11 days, when indoleacetic acid had shown a pronounced effect, but was only seen after 28 days. The slow action of the acidic auxins is not, therefore, due to slow entry into the plant.

That the slow action is also not due to photodestruction (cf. Algeus[4]) follows from the fact that the action of naphthaleneacetic acid, which is resistant to photo-destruction, is no more rapid than that of indoleacetic acid. To make this point certain, however, an experiment was carried out with the latter acid in which the solution was changed daily, instead of every 5–7 days as in the other experiments. There was no marked increase in the growth promotion, nor did it begin earlier. The slow reaction thus seems to be a characteristic of the system under study.

A substance which antagonizes the action of auxin in some assay systems, though not in all, is 2,3,5-triiodobenzoic acid. This compound was found to inhibit both elongation and cap formation. The effective concentration was 10^{-4} *M* and higher levels were toxic.

The isolated rhizoids (which contain the nucleus) behave somewhat differently. So far as auxin is concerned, the rhizoids are in most cases inhibited in elongation by added auxin at all levels down to 10^{-7} *M*. However, after the plants have been removed from the auxin solution and returned to unsupplemented Schreiber solution, they may afterwards show a striking growth promotion which lasts for several weeks. This is illustrated in Fig. 2. Such different behaviour to auxin by different parts *of a single cell* is of considerable interest.

The facts: (1) that the concentrations of auxin effective for the two actions are different and (2) that in some experiments, especially with methyl indoleacetate, cap formation was clearly promoted while elongation was not, suggest strongly that elongation and cap formation are independent processes. This supports previous conclusions as to their independence, based upon the evidence that cap formation is mediated by specific substances[17–19] and on the very different light-intensity requirements of the two processes[20].

It is well known that the addition of soil extract to sea water or to Schreiber solution ('Erdschreiber') promotes both growth and cap formation. This effect is evidently not the same as the action of auxin, as the following experiment shows. A group of plants in sea water with added naphthaleneacetic acid in a series of concentrations formed 55 per cent of caps in the optimal concentration (10^{-5} *M*)—a figure which

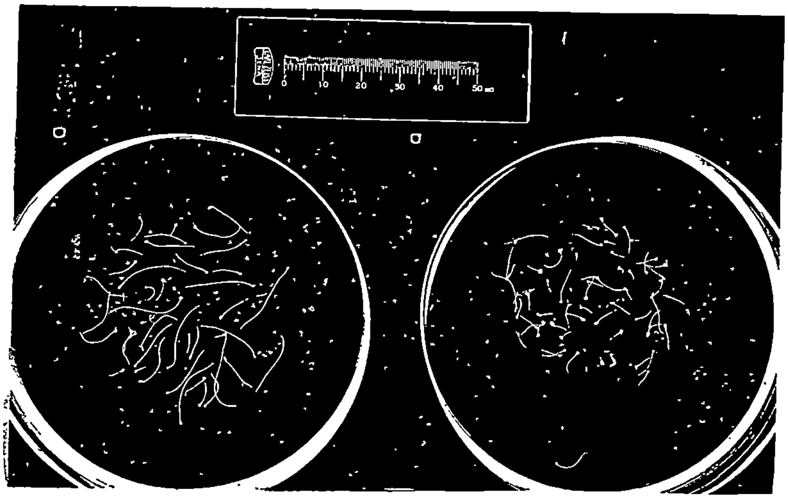

Fig. 2. Isolated rhizoids from plants pre-treated with indoleacetic acid 10^{-5} *M*, grown afterwards in Schreiber solution for 20 days

did not increase further in an additional 6 weeks. At this point Erdschreiber solution was added. Within one week the percentage of caps had risen to 90 per cent. Comparable increases occurred in the other concentrations. It is suggested that soil extract and auxin act upon essentially the same process but in different ways.

Some of our experiments point also to the probability that in bright light a growth-limiting factor is used up or destroyed, but that this factor can be synthesized from the constituents of Erdschreiber solution. This light-labile growth factor also cannot be identical with auxin.

Effect of Enucleation

Since in *Acetabularia* the single primary nucleus lies in the rhizoids, another, and a long-standing, problem of auxin action could be attacked. Many attempts have been made to demonstrate an action of auxin on *in vitro* systems, but always without success. In consequence, it appears that the intact cell is necessary for auxin action, and this has led to the speculation by one of us that the primary action of auxin may be exerted on the nucleus, which then secondarily modifies enzyme systems controlling growth. *Acetabularia* is one of very few organisms in which this proposal can be readily tested, because its enucleated cells can be easily prepared and they have been shown to survive well and even to grow. The action of auxin was therefore studied on enucleated *Acetabularia*. The part cut off in these experiments comprised the whole rhizoid plus about 1 mm. of stalk.

Enucleation slows down elongation very greatly. This fact, although mentioned by Hämmerling in 1934[17], does not seem to have been clearly brought out in subsequent work. However, the growth of enucleated plants is still readily measurable. From our experiments it seems clear that they still show some growth promotion in response to auxin, though the responses are smaller than those in intact plants. For example, elongation of enucleated plants (30 mm. long) in 3 weeks was increased from 2·6 mm. in the controls to 4·7 mm. in 10^{-4} *M* indoleacetic acid. Furthermore, the percentage of caps was increased from 14 (controls) to 44 (indoleacetic acid) in the same period. As an average of four experiments in Schreiber solution, cap formation in enucleated controls was 14 per cent and in optimal auxin 31 per cent (final figures reached); in an additional two experiments, however, there was no response to auxin. On the whole, it seems clear that indoleacetic acid does promote cap formation in enucleated plants, and it increases not only the rate of formation but also the final number of caps. In most cases a higher auxin-level was needed for the optimum effect in enucleated than in intact plants.

Additional evidence is supplied by the finding that triiodobenzoic acid, 10^{-4} *M*, inhibits strongly the formation of caps by enucleated plants. It can be concluded that both auxin and an auxin antagonist are able to act on the cytoplasm. Whether or not the nucleus makes the action more effective must be left open.

In general, our experiments indicate that auxin plays a growth-promoting part, rather than being itself one of the previously postulated morphogenetic substances. Since it does not increase cap formation when applied to old plants which have already begun to form caps, it cannot be the cap-forming substance itself. It cannot be the precursor which is converted to cap-forming substance by bright light[19,20], because if so it should always (in optimum concentration) produce 100 per cent caps in bright light. For the same reason it can scarcely be any earlier intermediate in the chain. Therefore it must act only to promote one or more of the reactions leading to cap formation. This role is comparable with the influence of externally applied auxin on elongation in *Acetabularia*, which is also only a promotion. The part played by endogenous auxin in these reactions will be a subject for further study. In the meantime, the fact that these effects can occur, albeit to a limited extent, in the absence of the nucleus, seems to us of importance for theories of auxin action.

This research was carried out during the tenure of a Guggenheim Fellowship by one of us (K. V. T.). Use of the facilities of the Naples Marine Station, and the helpful co-operation of the director, Dr. R. Dohrn, and his staff are gratefully acknowledged.

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LETTERS TO THE EDITORS

BIOLOGY

Fluorescence Effects from Corals irradiated with Ultra-Violet Rays

In January 1957, three months after the official inauguration of the Aquarium of Nouméa which my wife and I established in New Caledonia, we obtained the first effects of fluorescence through irradiation with ultra-violet rays of deep-water corals. The different specimens treated had been collected in the lagoon at a depth of 35–40 m., about twenty miles from our station where they are kept alive.

The first corals on which we experimented belonged mainly to the genus *Flabellum*, with which we obtained green fluorescence of great intensity. (There is no doubt that it is fluorescence, as the phenomena stop as soon as the excitation ceases. In other words, there is in these corals no residual photoluminescence, which becomes apparent as soon as the irradiation ends.) Since then, all specimens of corals, collected in the same region and elsewhere from varying depths, have been systematically exposed to treatment with ultra-violet radiation.

Our preliminary observations are as follows: (1) Only a certain number of species respond to irradiation. (2) All individuals belonging to the same genus produce generally the same colour of fluorescence (thus the *Flabellum* show greens, the *Trachyphyllia* oranges, etc.). However, certain genera may present several colours in the same individual. In that case a particular colour is always localized in the same region on each organism. (3) Colours and frequency-range are, at present: green, varying from light to dark, and at times with a glow; orange, varying from light to dark and at times with a brilliant glow; silver blue (very small range); reddish (either dull or shiny); beige (very small range); brown (very small range); and grey (sometimes silvery).

The definite green colour of certain corals may sometimes change to pink either after frequent or too lengthy exposures to irradiation or perhaps from other causes. (4) Only the fleshy parts of corals are fluorescent; the skeleton itself never reacts. (5) The expansion of polyps of certain species, especially those which expand normally in day-time, is greatly excited by ultra-violet irradiation, while species which expand at night do not react positively. (6) Most corals exposed to ultra-violet irradiation suffer from this treatment. In certain cases it may be fatal if the experiment is repeated too often or if it is of too long duration. Generally speaking, the intensity of fluorescence decreases day after day in proportion with the decreased vitality of the subject treated.

Other organisms collected from a depth of 35–40 m., particularly anemones and calcareous algae, show fluorescence, but its intensity is much less than that observed with corals.

Apart from the exceptional beauty of the fluorescent corals, the phenomena suggest research in different fields such as chemistry, physics and biology. Finally, this fluorescence might be a new approach to the systematic study of these corals. In fact, certain specimens which seem *a priori* to belong to the same species react to ultra-violet irradiation with quite different colours.

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Lumpy Skin Disease of Cattle in Kenya

Lumpy skin is an infectious disease of cattle characterized by the eruption of cutaneous nodules on any part of the body together with generalized lymphadenitis. It has been known for some time in several African territories, including Northern Rhodesia (1929)[1,2], Bechuanaland (1943)[3], the Union of South Africa (1944)[4], Southern Rhodesia (1945)[5], Mozambique (1946)[6], Swaziland (1946)[7], Basutoland (1947)[7], Madagascar (1954)[8] and Belgian Congo (1955)[9]. The dates of first confirmation in these countries are in parentheses.

To the above list must now be added Kenya, where the disease was recognized for the first time towards the end of 1957 on a farm in the Nakuru area. The source of infection in this outbreak is unknown. The disease was confined to calves, some of which were severely affected. The natural mortality was very low, and all active cases were slaughtered. After confirmation of the initial outbreak, field staff of the Veterinary Department carried out an extensive and systematic search for further cases of the disease over a wide area of the surrounding districts. Only a few active cases were found on widely separated farms. These were generally mild in character, and involved, as a rule, only one or two animals in each herd. Over the past year lumpy skin disease has spread slowly and sporadically despite the enforcement of stringent quarantine restrictions and sanitary arrangements. Cattle on recently affected farms in the vicinity of Lakes Nakuru and Elmenteita, however, have shown a higher morbidity, and individual cases have been more severe.

In Kenya, as in other affected territories, the spread of the disease has been unaccountable. Outbreaks have occurred in herds several miles apart with no evidence of infection on neighbouring or intervening farms. There was severe infestation by mosquitoes on the first farm where the disease was diagnosed. Infestations of varying severity have also been reported on 54 out of 56 farms afterwards infected by lumpy skin disease. The possible role of mosquitoes as vectors of the disease is under investigation.

In the more severe cases in Kenya nodules have been found not only in the skin but also in the internal organs, for example, oral cavity, pharynx, larynx, trachea, lungs, liver and proventriculi. Histological examination of skin and other lesions has revealed the presence of intracytoplasmic inclusions in a large proportion of cases in the epithelial and infiltrating mononuclear cells similar to those first described by Thomas and Mare[4].

Alexander *et al.*[10] have isolated three types of infective agents from cases of lumpy skin disease. One of these, their group II, produces a generalized response on the part of susceptible animals with the development of nodules over practically the entire body following subcutaneous inoculation of virus. In tissue-culture monolayers this agent gives rise to the rapid formation of large syncytia and the development of large intranuclear inclusions. Agents of this type have not, so far, been isolated in Kenya. Another type of agent, group III, rarely produces generalized skin eruptions on inoculation of susceptible cattle. In tissue culture the cytopathic changes develop more slowly than those of the first type and the inclusions are intracytoplasmic. Seven separate isolations of agents of this type have been made so far in this Laboratory from different farms, including the farm originally infected.

In addition there have been five isolations of a type of agent from active cases of the disease which gives rise to characteristic cytopathogenic changes in cell cultures but which elicits no clinical response whatsoever on inoculation of susceptible cattle. In this respect these resemble the agents of Group I as described by Alexander *et al.*[10].

Fuller details of the work carried out so far on lumpy skin disease in this Laboratory will be reported shortly.

We are grateful to the Director of Veterinary Services for permission to publish this preliminary communication.

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Dec. 23.

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Records of Young Eels in Kenya Rivers

Frost[1] published the first account of the biology of freshwater eels in Kenya. She showed that, of the three species of eel found in the easterly flowing rivers, *Anguilla nebulosa labiata* Peters is the most abundant above 3,000 ft.; *A. mossambica* Peters is comparatively rare, and *A. bicolor bicolor* McClelland is both uncommon and apparently restricted to the lower reaches of rivers. Our own (unpublished) records from the lower Sabaki (Athi) River and from upper tributaries of the Tana River confirm this distribution.

The elvers of *A. mossambica*, the common South African eel, are now well known, and runs up the Buffalo River (Eastern Cape) in February and March have been recorded for three successive years[2-4]. Recently, the elvers of *A. b. bicolor*, known previously only from Madagascar, were found at sea-level in the Mzinga River near Dar es Salaam (Tanganyika) in late January and mid-February[5]. With these elvers were two which could be referred to *A. n. labiata*, the first to be recorded. But apart from two rather damaged early stages (165 and 115 mm.) collected by Frost[1], the largest of which she tentatively assigned to *A. n. labiata*, there have been no records of elvers or young eels in Kenya rivers.

Table 1

Source	No. of specimens	Total length (mm.)	Ano-dorsal fin ratio		Vertebral count†
			Elvers	Adults*	
A. Merilla Barrage (Tana River) April 24, 1958	18	104–161	9·7–13·4	10·0–14·9 (*A. n. labiata*)	105–108
B. Jilore (Sabaki River) Nov. 1956	1	87·5	11·4	14·6 (*A. mossambica*)	91

* Based on Frost's Kenya collection (unpublished).

† Counts determined in *A* by dissection (one) and by X-ray photographs (five); in *B* by X-ray only.

In June 1957 we received reports of numerous 'elvers' having been found among the debris caught up in the draft tubes of the turbines at the Tana Hydro-electric Power Station on the Tana River, at an altitude of approximately 3,800 ft. (0° 40′ S.; 37° 14′ E.). Unfortunately no specimens were kept. However, further investigation in the vicinity of the power station in April 1958 produced eighteen young stages of eels which had been trapped in the syphon-priming chamber of the dam serving this power station (the Merilla Barrage), the construction of which device enables it to function as a very efficient elver trap. Subsequent visits have proved negative, but more young stages are expected in the appropriate season, which is probably during the 'long rain' floods of March–May in this area. The total lengths of the young eels (104–161 mm.) are considerably larger than the lengths of elvers recorded by Frost[5] at sea-level, suggesting that they are in fact post-elvers. Although apparently caught while migrating upstream, there is no indication of their date of arrival at the Tana River mouth, some 300 miles to the east, and it is also possible that they had remained in the priming chamber for some time. We have also been able to examine a much smaller eel (87·5 mm.) caught in a native basket-trap at Jilore on the Sabaki River (3° 8′ S., 40° 4′ E.) by Mr. John Kadenge, this locality being only 20 miles from the sea at an altitude of 100 ft. There is some doubt regarding date of capture, but it is believed to have been trapped during the 'short rain' floods of November 1956.

Adults of the three Kenya species of eel can be separated on the basis of dentition, coloration, the ano-dorsal fin origin formula used by Frost[1], and vertebral counts. These characters are not entirely satisfactory for the young stages, although vertebral counts are probably the most reliable.

Coloration. The eighteen Tana River eels were distinctly mottled, as are the adults of *A. n. labiata*, but after preservation in formalin or alcohol only the largest retained this coloration. The single Sabaki River elver, first inspected after about 18 months in formalin, showed a light peppering of chromatophores above the mid-lateral line, but no suggestion of mottling.

Dentition. As in adult *A. n. labiata*, the largest Tana River eels appear to have a slight groove between the lateral rows of teeth in both jaws, but in the smaller specimens and in the Sabaki River elver the teeth are rather irregularly placed.

(*Continued on p.* 971)

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FROM DAN TO BEERSHEBA: EXCAVATIONS IN NORTH AND SOUTH PALESTINE

Lachish (Tell ed-Duweir) IV

The Bronze Age. By Olga Tufnell. With contributions by D. F. W. Baden-Powell, Dorothea M. A. Bate, Jaroslav Černý, David Diringer, Madeleine Giles, Hans Helbaek, B. S. J. Isserlin, Margaret A. Murray, Barbara Parker, Edith Porada, F. C. Thompson, Eric Todd and John Waechter. Text: Pp. 351. Plates: pp. 6+96 plates. (The Wellcome-Marston Archæological Research Expedition to the Near East.) (London: Oxford University Press, 1958. Published for the Trustees of the late Sir Henry Wellcome.) 168*s*. net (text and plates).

Hazor I

An Account of the First Season of Excavations, 1955. By Yigael Yadin, Yohanan Aharoni, Ruth Amiran, Trude Dothan, Immanuel Dunayevsky and Jean Perrot. (The James A. De Rothschild Expedition at Hazor.) Pp. xxiv+160+184 plates. (Jerusalem: At the Magnes Press of the Hebrew University; London: Oxford University Press, 1958.) 168*s*. net.

THE appearance of Lachish IV brings to a close the immense task of publishing the results of six seasons of excavations at Tell ed-Duweir in southern Judea, and Miss O. Tufnell and her collaborators are to be warmly congratulated on their achievement. The excavations themselves ended in 1938 with the tragic death of their director, J. L. Starkey, and since then it has been the task chiefly of Miss Tufnell to gather together the records of the work and present them to the public. Previous volumes have given accounts of the Biblical city, the Canaanite temple, and of important epigraphic material. The present volumes trace the history of the *tell* itself and the neighbouring cemeteries from the Chalcolithic period until the destruction of the city by Israelites or Philistines about 1200 B.C. Although the only important structure described is the Middle Bronze Age glacis defence system, a wealth of material from the Early, Middle and Late Bronze Ages is carefully analysed, and an outstanding contribution is made to our knowledge of south Judean civilization during the third and second millennia B.C.

The most interesting sections deal with what Miss Tufnell calls the 'Caliciform culture' (Albright's Middle Bronze I, and Miss Kenyon's Intermediate Early–Middle Bronze). Miss Tufnell prefers to see in the differences between various groups of Caliciform pottery evidence for a chronological succession, rather than for different ethnic groups, as Miss Kenyon has suggested at Jericho. If the "straggling house walls" of the north-west settlement (p. 42) really belong to this period, then their plan (Plate 95) lends support to this theory, since they obviously belong to several superimposed building phases. It is a pity that these phases are not noted or analysed in the report.

It is not to be expected that this is an ideal publication. An interval of twenty years between excavation and report is too long, and Miss Tufnell has had to cope with another archæologist's records, which were, plainly enough, in many cases inadequate. The treatment of the north-east section, for example, is very sketchy, as is the drawing of the section itself, and consequently the discussion of the development of pottery types lacks that close stratigraphic control which is essential. In this respect the charts (Figs. 2–5) are especially suspect; sherd No. 123, for example (Fig. 3), from the 22-ft. level of the Middle Bronze glacis fill, looks very like a Chalcolithic bowl-rim. So, too, the references to the earliest material from Duweir—a Natufian end-scraper, a Neolithic painted sherd, and a grooved stone of Mesolithic/Neolithic type—are tantalizingly brief. There is enough evidence here to suggest that at the base of the mound the remains of a Neolithic community still lie buried.

The weakest point of the Lachish report lies in its arrangement. The student looking up comparative material is sent from page to page by a confusing series of cross-references and repetitions. Thus, there is a partial discussion of the Caliciform culture on p. 31 and a second, with new remarks, on p. 41; while the important group 1529 is treated on both p. 42 and p. 171 ff., and other groups of the same period on p. 153 ff. Similarly, on pp. 132–33 Prof. Černý reports on the Egyptian hieratic inscription on Lachish bowl III, while another opinion by Sir Alan Gardiner is quoted on p. 37. This leads to confusion and unnecessary labour.

Nevertheless, Miss Tufnell deserves great praise for publishing the material and records, however scanty, of this excavation. For many years to come these volumes will be one of the most important sources for the archæological history of Palestine. Their format is of the usual high standard of the Oxford University Press. I would make only one criticism: the form "ist", "iind", etc., for "1st", "2nd", is, to my mind, extremely ugly.

Tell el-Qedah is by far the largest (185 acres) ancient site in Palestine, and guards the main northern cross-roads in the Huleh plain. Its importance as the centre of Canaanite civilization in the north can be gauged from the number of times it is mentioned in Egyptian, cuneiform and Hebrew texts, and Dr. Y. Yadin and his army of assistants have now uncovered an impressive amount of the remains of this civilization, together with equally important remains of the Israelite period. Deserving of special mention are the pillared building of the time of Omri and Ahab (ninth century B.C.), the eighth century citadel, and the Late Bronze Age shrine, which, with its steles and cult-objects, throws a flood of light on Canaanite art and religion.

The wealth of archæological material found is here superbly presented, and this attractive volume is a credit to the Israeli printers and publishers responsible for it. I doubt, however, whether it is altogether wise to publish on so lavish a scale the results of the first of a series of excavation seasons. Dr. Yadin is himself aware of the drawbacks (p. xix), but considers them to be outweighed by the advantages of prompt publication. One cannot help feeling, however, that most of the important material could have been published in a series of more modest preliminary reports, leaving the final discussion of the major structural remains to a later date. An excavator's appreciation of the significance of his discoveries and of the history of his site must continually change with every new find. Even in Hazor I the evidence of later seasons is incorporated into the discussion at several points, for example, in the case of the Late Bronze Age shrine, while, conversely, the analysis of certain strata is left incomplete, to be discussed in a future volume. Promptness in publication is an admirable aim, but not if it means unnecessary duplication, especially when volumes are 8 guineas each.

Dr. Yadin's method of elucidating the history of Hazor has been to divide up his excavated areas vertically into a number of strata, each containing a complex of contemporary buildings. The criteria for establishing contemporaneity seem to be the plans of the buildings and the absolute levels of their floors. The strata are dated by the objects found therein. This method has undoubtedly established the broad outlines of the chronology of Hazor; but the treatment is really not as detailed as it could have been. Within any one stratum there are bound to be a number of sub-phases, which here usually pass unremarked. For example, the plan of area *A*, stratum VI (Plate CLXXIII) suggests that locus 76 was originally an open space between two buildings, and that the northern wall is a later addition. The exact sequence in this area could only have been ascertained by a much closer observation of the stratigraphy than the published report indicates. Again, it is axiomatic that all the material from one 'stratum' is not of equal value for the dating of that stratum. The pottery lying on the floor of a house will date from the last period of its occupation; the pottery from the deposit between one house and another above it may, according to whether that deposit is a destruction debris or a deliberate filling, either date the destruction of the lower house or the construction of the upper; while the latest sherds from the foundation trenches of a building will usually date its construction. Very seldom, if at all, are foundation trenches mentioned in this report. Pottery is said to come from a given locus, which is sometimes described as a room, a wall, a floor, etc.—sometimes, even, as 'undefined'—while the important fact, whether it comes from occupation material, debris, a deliberate filling, etc., is rarely stated. A curious instance of this failure to appreciate the significance of the exact provenance of finds occurs in the discussion of shrine I*A*, in area *C*. On p. 91 it is stated that a Cypriot milk-bowl of White Slip II type is one of the most significant sherds for dating the shrine. This bowl comes from locus 6062, which the plan (Plate CLXXX) shows to be a spread of small stones overlying wall 6134, the west wall of the shrine; this wall seems to have been destroyed at this point (it is shown only in broken lines on the plan, Plate CLXXXI). This stony spread is, according to the absolute levels printed on the plan, about 30 cm. above the top of wall 6134, and is surely one of the "several layers of small rubble stones" which on p. 75 are said to cover the slopes of the earthen rampart, west of the shrine, and to be either an intentional revetment or debris from houses above. In either case, this milk-bowl, and the sixteen other sherds published from the same locus, can scarcely be used as dating evidence for shrine I*A*.

Despite this lack of precision in the analysis of the stratigraphy of the site, this volume is most welcome as providing a yardstick for future work in Palestine. The drawings and the plans are excellent; especially is one grateful for the generous folders on which the plans are printed. The photographs are not so good. Too many of them have been taken in strong sunlight, which produces confusing shadows (for example, Plate VI, No. 6), while illustrations of objects *in situ* are of little use if, as is often the case here, the *situs* is not readily discernible in the picture. Fewer, better, photographs might have helped to reduce the cost of this report.

PETER J. PARR

"ARMS AND THE MAN"

No More War

By Dr. Linus Pauling. Pp. x+254. (London: Victor Gollancz, Ltd., 1958.) 16*s*. net.

The Devil's Repertoire *or* Nuclear Bombing and the Life of Man

By Victor Gollancz. Pp. 192+2 plates. (London: Victor Gollancz, Ltd., 1958.) 10*s*. 6*d*., cloth bound; 5*s*. paper covers.

The Arms Race

A Programme for World Disarmament. By Philip Noel-Baker. Pp. xviii+579. (London: Atlantic Book Publishing Co., Ltd., 1958. Distributed by Stevens and Sons, Ltd.) 25*s*. net.

THESE three books are essentially variants on the thesis that the advent of the nuclear bomb has made the renunciation of war inevitable if mankind, let alone civilization, is to survive. The thesis is stated succinctly by Dr. L. Pauling in his preface, but the level of that preface is scarcely sustained, and even the scientist may find Dr. Pauling's the least satisfactory book of the three. It is indeed addressed to the non-scientist and successive chapters explain in non-technical terms for the general reader the nature of nuclear weapons, what is meant by radioactivity and fall-out, the relations between radiation, heredity and disease. The facts about fall-out are summarized in a separate chapter, which, while not attempting to conceal the incompleteness and contradictions in existing knowledge, strongly supports the recommendation of the Committee on the Biological Effect of Atomic Radiation set up by the U.S. National Academy of Sciences—National Research Council that exposure to radiation should be kept as low as possible. After explaining, in a chapter on the nature of nuclear war, the reasons for his fear that such a war would mean the end of civilization, Dr. Pauling surveys in the following two chapters the several appeals for peace made by scientists and the need for international agreement. Finally, he outlines his own proposal, namely, research for peace.

He suggests that a World Peace Research Organization should be set up within the United Nations to study how to solve great world problems of the kind that have in the past led to war, including an attack on the problem of preventing the outbreak of a nuclear war by design or by accident. Dr. Pauling visualizes such an organization, after a thorough analysis of the problems involved in an international agreement to stop all testing of nuclear weapons, formulating a system offering the maximum safety and the least risk of violation, and he is prepared to place at the disposal of the organization a staff of some 2,000 specialists within two years, a figure which might rise to 10,000 within a decade, and puts the cost of the proposal as initially some 25 million dollars a year and ultimately 100 million dollars. He argues that if world problems were attacked in this way, imaginatively and with original methods by outstandingly able investigators, there are great possibilities of progress and of discoveries which would make the outbreak of a nuclear war far less likely. Except in its scale the proposal is scarcely novel, as the work of the Institute of Pacific Relations has shown for a quarter of a century.

Dr. Pauling is convinced that such an organization would repay its cost in savings in defence budgets and in other ways, and points out that the sum he contemplates is only a small fraction of the military budget of even one country such as the United States or the U.S.S.R. He does not, however, quite meet the point of urgency that is one of the critical aspects of the situation, nor what is implied in the diversion of such a proportion of the world's limited resources in highly varied scientific man-power to this constructive purpose. If the nations were prepared to take that immediate step, may not some more direct action in regard to disarmament be possible now ?

The interest of the book to the scientist lies largely in these last chapters and, while its bibliographical references are rather scanty, it reproduces the Mainau Declaration of Nobel Laureates of July 1955, Schweitzer's declaration of April 1957, and a statement of Einstein's which are convenient for reference. Dr. Pauling does not, of course, ignore the moral aspect, and he argues in conclusion that the use of nuclear weapons is immoral and that morality must now take its proper place in the conduct of world affairs. This, however, is the essence of Mr. Gollancz's book, which presents persuasively, sensitively and with real felicity and sincerity the spiritual and moral issues involved, taking the thesis one step further to argue for unilateral nuclear disarmament. Mr. Gollancz does not shrink from what might be involved in such a step, but no more than Dr. Pauling does he really face some of the real practical difficulties or the moral issue of involving others in the consequences of a unilateral decision.

In this respect, the major contribution comes from Mr. Philip Noel-Baker. Much the longest of the three, his book considers nuclear disarmament as a facet of general disarmament and in the light of the experience gained in the long negotiations for disarmament under the League of Nations. Mr. Noel-Baker is convinced that much of that work is relevant to present problems, and without disguising the need for anxiety and urgent action he takes a hopeful view of the possibilities. The scientist will find much of interest in this lucid, well-documented and authoritative survey; not least, a compelling demonstration of the futility of military or defence research. The argument is realistic, without ignoring or despising the moral argument, and although it does no more than outline the broad stages by which disarmament should proceed, it calls just as incisively as Dr. Pauling for bold and large steps, including the abolition of military research, and for the patient and determined pursuit over many years of new policies and reforms based on known facts, which the recently established Institute of Strategic Studies could well help to disseminate. R. Brightman

MODERN MIND

The Emergence of the Modern Mind

Edited by Prof. Frederick C. Gruber. (The Martin G. Brumbaugh Lectures in Education.) Pp. 93. (Philadelphia: University of Pennsylvania Press; London: Oxford University Press, 1958.) 20*s.* net.

THIS book consists of the four Martin G. Brumbaugh lectures given at the University of Pennsylvania in 1957. They are popular lectures, designed mainly for students of education. Prof. Conway Zirkle, writing on "Our Biological Inheritance", paints a lively but gloomy picture of man as the most successful of animals, yet ill-adapted to the cultures he has produced; knowledge has grown too big for us, our work is dull, civilization is a strain from which the human animal sometimes seeks violent escape; perhaps hope is possible when we look back in history and see what catastrophes we have survived or consider what further successful adaptations we may achieve in the next half million years; we may even survive some of our present world-views. Prof. Edel, on "The Greek Image in American Thought", emphasizes the freshness of Greek thought for Western civilization and our need to look back to the Greeks for new ideas. He is scornful of those bolstering up reactionary philosophies by skilful quotation from Plato. The Greeks must be approached in their own spirit of free inquiry; the questions they discussed are the ones we find important; as an example Edel gives a skilful analysis of the underlying assumptions of democracy, looked at in the light of Plato's "Republic".

The other two lectures are less interesting. Prof. Ethel Alpenfels's essay on "The Mind and the Mores", is very slight; she applies the social anthropologist's view of culture to American 'folkways and mores'; but she never makes it clear how far human beings are 'determined' by their cultures and how far they are free individuals capable of independent thought. Prof. Percy Miller's picture of "Nineteenth Century New England and its Descendants" would be of more interest to Americans than to Britons; his references are too off-hand for us to judge the relevance of his criticisms; and although he wants to show us the greatness of Henry Thoreau, he does not tell us enough about his life, work and writings to convince.

It will be noticed that the link between these essays and the title of the book is tenuous, but this is not important. Although there is nothing original in these lectures and the writing is sometimes pretentious or naïve, they are on important topics and would have a stimulating effect if used, for example, in the sixth forms of grammar schools as a basis for discussion. T. H. B. Hollins

NEUROPHYSIOLOGY OF BEHAVIOUR

Ciba Foundation Symposium on the Neurological Basis of Behaviour

Edited by G. E. W. Wolstenholme and Cecilia M. O'Connor. (In commemoration of Sir Charles Sherrington, O.M., G.B.E., F.R.S., 1857–1952.) Pp. xii+400. (London: J. and A. Churchill, Ltd., 1958.) 52*s*. 6*d*. net.

THIS volume contains a collection of some nineteen papers presented at a Ciba symposium commemorating the birth of Sir Charles Sherrington in 1857. As is usual with Ciba symposia, the meeting was attended by only a small international group, and the book is intended to present the proceedings to a much wider circle. The papers covered many fields related to neurology, but the main emphasis was, as might be expected, on neurophysiology and experimental neurology.

The latest data on the activity of single neurones of the spinal cord are reviewed by Eccles, while the behavioural effects of lesions (Bard, Brierley, Kluver) and electrical stimulation, both in animals (Olds, Andersson, Monnier) and in man (Penfield) are very adequately covered. Other fields discussed are: sexual behaviour (Harris), the effects of stress (C. P. Richter), the rhinencephalon (Green), brain enzymes (Rosenzweig) and drug action (Elkes). Many of the papers are reviews containing material much of which has already been published; nevertheless they serve to bring this together for discussion, which follows each paper. On the other hand certain papers contain a proportion of new information, and these, while they illustrate trends in research, also focus attention on the fact that new developments in this field must depend upon advances in technique. For example, Olds outlines the new results which are coming from experiments on electrical self-stimulation in animals; Jasper reviews the responses of single cortical neurones in unanæsthetized animals during conditioning; and Malcolm discusses the activity of cortical neurones in freely moving animals. All these developments and many others which are providing information linking electrophysiological and behavioural studies depend upon new technical skills.

The only criticism which one might make is that the contributions made by psychology and biochemistry to this symposium are small, yet both these fields of study are becoming increasingly important to work on neurological mechanisms. However, no symposium can ever be truly comprehensive if it is to be confined to a single volume at a reasonable price, and this book provides an excellent review of our present state of knowledge in this subject. It is well illustrated and contains an adequate index.

P. B. BRADLEY

PHYSIOLOGY OF THE CEREBELLUM

The Physiology and Pathology of the Cerebellum

By Prof. Robert Stone Dow and Prof. Giuseppe Moruzzi. Pp. xv+675. (Minneapolis, Minn.: University of Minnesota Press; London: Oxford University Press, 1958.) 100*s*. net.

STUDENTS of cerebellar physiology have been well served by a sequence of splendid critical writings, each marking a distinct advance in knowledge, and in some degree defining the direction of later research. Foremost among them stand those of Sherrington (1900), Luciani (1915), Bremer (1935) and Holmes (1939). Dow and Moruzzi's new book will take its place with these. A physiological and pathological study of the cerebellum, it is planned as companion to a forthcoming morphological treatise by Larsell.

In their general nature, and in the technical approach to them, cerebellar problems resemble those presented by other parts of the central nervous system, but without preoccupation with the relation between nervous and mental events. The oldest approach tries to analyse the disorder of function—in this case, of posture and movement—resulting from destruction of the cerebellum or of some part or parts of it. Following the injury, the pattern of disability undergoes progressive change until a final steady state is reached. It is difficult to determine how far the disability at each stage is 'negative', due to lack of cerebellum, and how far 'positive', due to new activity of surviving nervous tissue. The general conclusion, however, is that the cerebellum tends to subdue postural reflexes on one hand, and on the other, to reinforce and steady the motor outflow from the brain. Electrical stimulation, although its effect is mixed, confirms the reality of these two streams of action.

The large and richly folded cerebellar cortex (with an area only a small fraction of which is exposed on the surface of the organ) receives impulses from all the receptors, and not only from the proprioceptors, as would have been expected from pioneer work. These impulses arrive at areas the surface localization of which is sharpest in deep anæsthesia. The cortical Purkinje cells send impulses to the cerebellar nuclei and thence to brain and cord. How far is this cortical output directly driven by the afferent input, and how far by intrinsic neuronal activity of the cortex? This cortex has the same apparently homogeneous, but very complex, microscopical structure throughout its extent. In the past there has been some loose usage of the term 'functional localization'. Anatomical localization of areas of arrival and departure of impulses has been abundantly shown. Is the active response of the cerebellar cortex to incoming impulses also localized, or is there, rather, spread and mass action, converging ultimately upon the different corticofugal systems?

On these and many other questions, this book assembles a wealth of experimental and clinical fact. The bibliography has about 2,000 references, old as well as new, and in many languages. These are not merely quoted, but critically appraised: the authors have taken great trouble to extract from them the facts needed for reasoning, and to reject poor observations (for example, those with inadequate anatomical control). The arrangement is methodological: ablation experiments; stimulation experiments; electrophysiological experiments; the cerebellum and other central structures; clinical symptoms; pathology. The analysis of clinical symptoms reveals the full stature of Gordon Holmes's contribution to cerebellar physiology. The pathological processes affecting the cerebellum are admirably described from the physician's point of view. Some of the sections end with interesting general essays, and these, and the essay "General Considerations on the Function of the Cerebellum", might well be read consecutively. The book as a whole would probably not be read consecutively by anyone other than a reviewer; but it is all very readable, well indexed and well supplied with cross-references. Its great virtue is that it proclaims the important matters on which we are ignorant, and does not somehow convey the idea, as other writers on the nervous system, no doubt unintentionally, have sometimes done, that our understanding is all but complete. By this frankness it hopes, and is likely, to stimulate research. It is the fruit of more than twenty years practical work, thought and reading by both authors. It could not possibly be mistaken for a mere journalistic compilation. C. G. Phillips

CLINICAL AND EXPERIMENTAL CANCER RESEARCH

Carcinoma of the Lung

Edited by J. R. Bignall. (Monographs on Neoplastic Disease at Various Sites, Vol. 1.) Pp. xii+298. (Edinburgh and London: E. and S. Livingstone, Ltd., 1958.) 55*s*. net.

Variables Related to Human Breast Cancer

By A. Elving Anderson, Harold O. Goodman and Sheldon C. Reed. (A Study from the Dight Institute of Human Genetics.) Pp. xiii+172. (Minneapolis, Minn.: University of Minnesota Press; London: Oxford University Press, 1958.) 32*s*. net.

Proceedings of the Second International Symposium on Mammary Cancer

Held at the University of Perugia, 24th to 29th July, 1957. Edited by Lucio Severi. Pp. liv+871. (Perugia: Division of Cancer Research, 1958.) 12,000 lire; 145*s*.; 20 dollars.

THREE recent books illustrate a current trend towards the detailed study of neoplasia in particular organs or tissues in human beings as well as in animals. Carcinoma of the lung is the subject of the first of a series of monographs designed to cover the range of neoplastic disease in special sites. The series is based primarily on the first-hand clinical experience of a group of postgraduate teaching hospitals in London supplemented by expert aid from other sources. The present volume, reflecting the practice of the Royal Marsden and Brompton Hospitals, includes a discussion of etiology, occupying about one quarter of the whole, by R. Doll. Dr. Doll expounds his views on the etiological importance of cigarette-smoking lucidly and persuasively. The weakest link in the argument seems to be the identification of the mechanism of carcinogenesis; the evidence for decisive operation of carcinogenic hydrocarbons is unconvincing. The main thesis rests on information about what actually happens in human beings, and although Dr. Doll is convinced by the evidence incriminating cigarette-smoking, he recognizes that inconsistencies persist and that interpretation is difficult.

The intrinsic hazards in the study of the etiology of human neoplasia are well shown in a report from Minnesota of a careful and critical investigation of the role of genetic factors in cancer of the human breast. The authors give especial attention to the validity of research methods; many previous investigations are clearly inadequate. Their own conclusions are cautious. They find good evidence that mothers, sisters and daughters of breast-cancer patients are about twice as liable to cancer of the breast as other women of similar age, and that the enhanced liability does not apply to cancer at other sites. Genetic factors are probably involved in the etiology of human breast cancer but are less important than non-genetic factors. These investigators are not satisfied that information now available about such factors as marital status, number of pregnancies and breast-feeding is sufficient to justify the advocacy of prophylactic measures, and they show a welcome recognition of the danger of meddling with the lives of human beings on the basis of imperfect and incomplete understanding of neoplastic processes in the breast.

The limitations of knowledge are also evident in the report of the Second International Symposium on Mammary Cancer held in Perugia in 1957. More than eighty contributions from fifteen countries cover a wide range of observations and opinions, human and animal studies being about equally represented. The endocrine aspects of mammary cancer receive most attention. Although there is wide agreement among the contributors that hormones are important in the etiology of cancer of the human breast, the mechanism of their action is not known. Moreover, the endocrine management of advanced breast cancer remains almost wholly empirical. These matters call for the closer integration of clinical and experimental research which this valuable symposium was designed to encourage; the clinical and experimental approaches are complementary and not alternative or competitive. The report scarcely does justice to the value of a symposium that brought clinical and laboratory workers together for informal discussions as well as formal expositions, but it is welcome, nevertheless, as a record of current thought and research on mammary neoplasia. All three books may be commended as valuable contributions in their several ways to the study of a subject of great complexity. L. Foulds

MECHANISM OR VITALISM?

The Physical Foundation of Biology

An Analytical Study. By Prof. Walter M. Elsasser. Pp. x+219. (London and New York: Pergamon Press, 1958.) 30*s*. net.

THE conflict between mechanistic and vitalistic philosophies has never quite subsided. Biologists, who on the whole have a profound respect for the senior physical sciences, tend to hold mechanistic views, at least as a working hypothesis, while physicists, knowing rather more of the limitations of their own discipline, are more inclined to assign special properties to living organisms. Prof. W. M. Elsasser, whose professional domain is magneto-hydrodynamics, has taken great pains to survey those phenomena displayed by living creatures which can be described in mechanistic terms, so as to identify the residue of functions which, he asserts, cannot be effected by physical means. For phenomena in this class, which cannot be interpreted in terms of pure mechanism, he proposes the term 'biotonic', which he defines as "Any causal relationship which involves an increase of information content in the system with the passage of time". The most prominent member of this class, he suggests, is organic growth of information, and he tries to show that neither genetic nor cerebral information can conceivably be "stored" in a physical sense, because of the minute scale of the structures involved—the chromosomes of the gametes or the nerve tissue of the brain. In an artificial computing machine there may be several grades of storage register, giving different degrees of capacity, accessibility and permanence, each fulfilling particular functions, and exploiting various physical effects such as ultrasonic vibration, electrostatic induction, and magnetic induction, apart from the familiar records in printed or punched cards. The total information storage capacity of a large computer may be quite imposing but does not approach the order of information contained in a human organism which, Elsasser suggests, may be as high as a thousand million bits. If a storage register of this capacity were required, the physical size of the storage system would have to be reduced, and a point would be reached at which the random variations of the system, the Brownian movement, or noise-level, would be of the same order as the magnitude of the stored signals. In such conditions, so the argument runs, the inevitable loss of information or ambiguity can be made good only by redundancy in the form of repetition or reduplication, which requires still more storage space, and so on. The conclusion reached is that no mechanical storage system can be imagined, still less constructed, which would contain enough information to specify the development or the mentality of a human organism. In the special case of human memory a particular difficulty, according to Elsasser, is that "There is no anatomical evidence for a storage organ", and also, "brain physiology has not brought to light any evidence for . . . special scanning devices" which, according to engineering principles, are needed for the selection and distribution of large stores of information.

Thus, proceeding from the Bergsonian idea that "the deviation of organisms from mechanistic behaviour ought to be studied in terms of the failure of information storage", this eminent and scholarly physicist develops a logical and consistent argument in support of the notion of epigenesis, claiming that the existence of biotonic laws is justified by the principle of finite classes which prohibits logical decisions involving operations in immense classes.

The argument is not easy to follow, and the reader's confidence is strained by the intrusion of several errors and oversights, particularly in the sections on neurophysiological data; neither the velocities nor the durations of nerve impulses are limited to the ranges quoted, and their strict relation to impulse wave-length should have directed the author's attention to the logical inconsistency in this paragraph. There is in fact some evidence of a scanning or space-time transforming mechanism within the brain, as well as of considerable redundancy in both genetic and cerebral structures. Not all matings are fertile, and many have monstrous issue ; by no means all memories are true, many are redundant and all are fragile.

In spite of the author's reasonable doubts, the storage capacity of a statistically assembled system of ten thousand million elements is not easy to estimate, and it may well be that in free permutative combination the figure would be of the required order. The same consideration applies to the inter-connexion of radicals in the nucleo-protein systems of chromosomes ; our present lack of complete factual knowledge does not seem to justify a philosophical denial of the possibility.

In a book of this size and scope, a subject index would have helped to restore biotonic energy, but there is an excellent summary in a few pages.

W. Grey Walter

BIOLOGICAL ULTRASTRUCTURE

Biological Ultrastructure

By Arne Engström and J. B. Finean. Pp. ix + 326. (New York : Academic Press, Inc., 1958.) 8 dollars.

The appearance of a new book in this rapidly developing field is greatly to be welcomed. During the past ten or so years an extraordinarily high degree of success has attended the application of various biophysical techniques and ideas to the study of molecular biology, and the time is certainly ripe for these developments to be recounted in generally accessible form. In the work under review, Prof. Engström and Dr. Finean have gone a considerable way towards doing this. The book commences with a section on "Methods in Ultrastructural Research", followed by an admirable account of "Principles of Molecular Structure", and succeeding sections consider the role of proteins, lipids, carbohydrates, nucleic acids and mineral salts in biological systems, in each case working up from simple molecules to the complex structures which they form in living material. This is an ambitious project, and in a book of this size, much can be treated only in general outline. Nevertheless the work will provide a useful introduction to the field for students, and others, particularly if used in conjunction with the earlier monograph by Frey-Wyssling, where greater emphasis is placed on cell structure. There are, however, a number of points in the book where one feels that considerable opportunities for arousing interest and enthusiasm have been missed, and where the summaries of recent developments seem lacking in colour and emphasis.

The section on the preparation of specimens for the electron microscope may leave the newcomer unaware of the dominating and almost unbelievably successful part played by studies on sectioned material in contemporary work, despite the technical details which are given of the methods used. The section on X-ray diffraction contains no mention of the fact that helical structures give a specific type of diffraction pattern ; and the omission of any account of hydrodynamic, light-scattering and optical rotation techniques could be criticized.

The section on proteins contains a great deal of useful information attractively presented, but in the treatment of chain configurations, the key part played by the recognition that the X-ray diffraction pattern given by synthetic α-polypeptides was that of a non-integral helix, which could be computed elegantly and in detail, and which agreed closely with that given by the Pauling–Corey α-helix, is slurred over ; and as a result one is left with an impression of vagueness which does less than justice to the evidence. Greater emphasis might also have been given to the importance of the successful application of the heavy-atom technique in X-ray diffraction studies of crystalline proteins.

Muscle and nerve are well covered (although a more extensive discussion of unmyelinated fibres would have been welcome) and the section on lipids is excellent. The section on nucleic acids is rather short in view of the elegance and interest of much recent work in this field. The genetic implications of the specific pairing of the bases required by the Crick–Watson double-helix structure for deoxyribonucleic acid are, surprisingly, not mentioned at all, and the recent work on tobacco mosaic virus, a superb example of the success, interest and importance of careful and detailed X-ray diffraction studies, is summarized only very briefly, and incorrectly; there is no mention of X-ray work on spherical viruses. On the other hand, the section on the role of mineral salts is extremely interesting and informative.

The principle of giving references, in general, only to key works containing more complete bibliographies has some advantages, but may sometimes leave the reader in the position of having come across tantalizing pieces of information which he can follow up, or the authority of which he can check, only by a prolonged search through the literature.

Despite these criticisms, the book remains a most useful introduction to the subject, and the authors are to be congratulated for their labours in bringing together so much information into one convenient volume. H. E. HUXLEY

CLASSIFICATION OF THE DIGENETIC TREMATODES

Systema Helminthum

By Prof. Satyu Yamaguti. Vol. 1: The Digenetic Trematodes of Vertebrates. Part 1: Pp. xi+1–980. Part 2: Pp. iii+981–1575. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1958.) 90 dollars; £34 the two parts.

SATYU YAMAGUTI has spent nearly thirty years on the production of his "Systema Helminthum", the first volume of which has now appeared. His work therefore commands the highest respect. Essentially, the book is a compilation of diagnoses of 102 families, 355 sub-families and 1,024 genera of digenetic trematodes, followed by a list of 4,037 references to the original literature, 1,302 illustrations grouped in 106 plates, and an index of the names of taxonomic units and their authors taking up rather more than 130 pages of two columns each. For the assembly of this tremendous fund of information Yamaguti merits high commendation. The diagnostic data are presented in Part 1 under the headings of definitive hosts—fishes, amphibians, reptiles, birds and mammals—which is a useful arrangement so long as it is realized that related species, and even one and the same species, may utilize more than one class of host. The entire taxonomic scheme is set out in Part 2 as an alphabetical list of families, sub-families and genera, whereas the arrangement in Part 1 is neither alphabetical nor the order in which groups may be separated by means of the keys provided. It is disconcerting to the reader to find this apparent disarray; he is prompted to ask why, for example, the relative order of the important families Plagiorchiidae, Lecithodendriidae, Microphallidae, Opisthorchiidae and Paramphistomidae should be 12345 for reptiles but 41325 for fishes, 52431 for amphibians, 14325 for birds, and 12435 for mammals. An alphabetical list has the virtue of ease of reference, even if it does leave unconsidered important questions of affinities.

The classification of the Digenea has generally been on the basis of comparative morphology of the adults, but G. R. La Rue (*Exp. Parasitology*, 6, 306; 1957) has revived the method of utilizing developmental data. His scheme recognizes super-orders, orders, sub-orders, super-families and families and is based particularly on the development of the excretory vesicle and associated parts. Many helminthologists will hesitate to accept it, on the grounds that both larval and adult characters are necessary for the delineation of genetic relationships. As Yamaguti has dealt mainly with adult characters, we can scarcely expect his scheme to provide more than just a list of families. What is striking is the great inequalities of families in this scheme; 13 of the 102 families comprise 10–25 sub-families and 21–106 genera each, making totals of 201 out of 355 sub-families and 551 out of 1,024 genera. At the other extreme, 59 families contain no more than four genera each; 31 of them contain one genus only, 13 contain two genera, 9 three genera and 6 four genera. This aggregate of families comprises only 108 genera and only 30 sub-families are represented. The 30 families yet to be considered have more than four genera and fewer than 10 sub-families each, and we may presume that they comprise 365 genera and 124 sub-families, 16 of the latter with only one genus.

The distribution of Digenea in the classes of host is also unequal; 54 families are represented in fishes, 13 in amphibians, 28 in reptiles, 29 in birds and 36 in mammals. The total exceeds 102 because 58 families are represented in two or more classes of host; the actual number of overlaps is 91, of which 15 involve fishes, 13 amphibians, 21 reptiles, 21 birds and 21 mammals, and the actual number of families involved is 33. Of the families containing one genus only, only the Orchipedidae occurs in more than one class of hosts (birds and mammals); of the remainder, 16 are represented in fishes, 0 in amphibians, 3 in reptiles, 3 in birds and 8 in mammals. The total numbers of families represented in one class of host only are 39 in fishes, 0 in amphibians, 7 in reptiles, 8 in birds and 15 in mammals. Families restricted to two or three classes of hosts number 1 in fishes and amphibians, 3 in fishes and reptiles, 3 in amphibians and reptiles, 1 in reptiles and mammals, and 11 in birds and mammals, and also 4 in fishes, amphibians and reptiles, 1 in fishes, reptiles and birds, and 3 in reptiles, birds and mammals. One family, the Echinostomatidae, is represented in four classes of hosts (fishes, reptiles, birds and mammals), and 5 families are represented in all five classes, namely, the Lecithodendriidae, Opisthorchiidae, Paramphistomidae, Plagiorchiidae and Microphallidae.

A work of this sort could scarcely be free from blemishes of one sort or another. There are many simple misspellings. Fig. 752 (Plate 62) and 1126 (Plate 93) are mislabelled *Pseudopsilotrema*, a name which does not appear in the index, and the names *Saccocoelium* and *Diphterostomum* are misspelt in various places. Many special citations made in the text are not supported by references in the list. For example, the reader's appetite is whetted on p. 184 concerning certain developmental features, a reference is cited and he is invited to see p. 371, where more recent information is given briefly in a second citation; he is then chagrined to find that the second reference is not supplied. Much more serious is the omission of any data concerning the sizes of trematodes and their organs and parts. No pretence is made of dealing with species beyond listing their names and, admittedly, ranges of size are difficult to specify for genera. However, genotypes are specified, and space would have been made available for size data had generic diagnoses been pruned of many redundant expressions which occur in them. Otherwise, some indication of size should have been given with the figures. The terms used in the text to denote size are useless because undefined. One solitary figure (7, Plate 1) has a scale; 1,301 figures leave the reader baffled regarding size. The figures of *Heterophyes heterophyes* and *Fasciolopsis buski* are about 55 mm. and 52 mm. long, respectively, whereas actual lengths may be 2 mm. and 75 mm. A reader having no foreknowledge of actual differences in size between trematodes may be greatly deceived by the figures, some of which are excellent but others are very poor and too small to be serviceable. He will also be disappointed in the general account of the digenetic trematodes, which barely covers one page and might have been amplified to an interesting and useful statement.

In spite of its shortcomings, the work will be much appreciated by all those who are concerned with trematodes, and its publication is at the same time a remarkable achievement and a notable event. The book summarizes most of the laborious and tedious systematic work which has been carried out, but it does indicate to the enlightened initiate how much research of a synthetic nature remains to be done. BEN DAWES

HARMONIOUS HERPETOLOGY

A Field Guide to Reptiles and Amphibians of the United States and Canada East of the 100th Meridian

By Roger Conant. (The Peterson Field Guide Series.) Pp. xv+366+40 plates. (Boston, Mass.: Houghton Mifflin Company, 1958.) 3.95 dollars.

DESPITE the number of books that already exist on North American herpetology, until now there has been no up-to-date survey and guide to the reptiles as well as the amphibians of that continent. For many years the little book of Schmidt and Davis provided an accurate guide to the snakes, but with the changes that have taken place in the nomenclature and taxonomy of American herpetology there became an urgent need to revise the "Field Book of Snakes" or replace it with another guide. In 1957, there appeared the "Handbook of Snakes" by Wright and Wright, but in two bulky volumes it could scarcely be considered a substitute for the earlier field guide. The book produced by Roger and Isabelle Conant is the answer to the urgent demand; it is remarkable in that it covers not only the snakes but also all the reptiles and amphibians that are known to occur in North America east of the 100th meridian and yet is of a handy pocket size and is reasonably priced.

The tradition of the Peterson Field Guide Series of combining scientific accuracy with readability has been maintained in this latest volume. In Britain many people are familiar with the "Field Guide to the Birds of Britain and Europe", by Peterson, Mountfort and Hollom, and some may be acquainted with the companion volumes on American birds; all praise the success and outstanding merit of these guides. The field guide to reptiles and amphibians of eastern North America, however, contains several special virtues. The inclusion of distribution maps in the guide to the British birds was at that time an unusual feature, but their value was at once acknowledged and the habit of including maps in check lists and field guides spread to other works. The Conants' book provides a series of well-executed maps which are confined to the end of the book and on which are shown the range of each species and subspecies discussed in the text, so that a check list for any region, state or county can easily be compiled. The photographs are of a superb quality and Mrs. Conant is to be congratulated on the excellent results of her painstaking task of hand dyeing more than 400 of them. Many of the original illustrations were seen by the reviewer, when it was evident that Mrs. Conant had spared no effort in achieving accuracy in colour and detail. Only live animals were photographed. A little of the brilliance of a few of the original illustrations has been lost in reproduction yet no one can deny that for identification purposes the best photographs and colour plates of American reptiles and amphibians are to be found in this book.

The format is essentially the same as in the other guides in the series. Specimens can be identified from the illustrations, with the aid of the salient features of the species listed on the facing page, or from the text where under each species are guides to the identification with notes on voice (in the case of the frogs and toads), size, similarity with other species, and range. Habitat notes and information on habits and natural food are given where known.

The introduction, and the chapters on the techniques employed in collecting reptiles and amphibians, on transporting the specimens, on snake-bite and its treatment, and on the care of the animals in captivity are highly commendable. Although most people will agree on the clumsiness of the term "reptiles and amphibians" when it occurs several times on one page, some purists will be disturbed to find it abbreviated to "herptiles" in this book. Nevertheless, Roger Conant's style is refreshing in its simplicity, and the expressiveness of his descriptions of the mating calls of frogs is worthy of special praise. The voice of the western chorus frog, *Pseudacris t. triseriata*, is likened to the sound produced by "running a finger over approximately the last twenty of the small teeth of a good-quality pocket comb, rubbing the shortest teeth last". Other mnemonics for frog calls range from "loose banjo strings" to "high pitched riveting machines".

"A Field Guide to Reptiles and Amphibians of the United States and Canada East of the 100th Meridian" is an essential companion to the collector of American "herptiles", to those whose interests are in the realms of systematics and behaviour and who require a dependable guide to the identification of the American species and also to the beginner in herpetology.

Mr. Conant has achieved success with his field guide to the eastern species. It is hoped that he will be persuaded to tackle with the same courage and patience a field guide to the herpetofauna of western North America. A. G. C. GRANDISON

THE ART OF GRAFTING

The Grafter's Handbook

By R. J. Garner. Revised edition. Pp. 260+32 plates. (London: Faber and Faber, Ltd., 1958.) 25*s*. net.

DURING the eleven years that have elapsed since the publication of the first edition of "The Grafter's Handbook" there has been ample proof of its value not only as a long-awaited text-book for the student, but also as a reference book for the practical horticulturist and nurseryman.

There can be little doubt that this revised and enlarged edition will receive an even more enthusiastic welcome, for it covers in detail all known methods of grafting. For those who wish to study seriously the theory and practice of this most fascinating of the gardening arts there is a full description of the methods, their advantages and uses. The author is to be congratulated on the way he has combined the results of his long experience as a practical propagator with the findings of modern research, in which he himself has played an important part at the East Malling Research Station.

A review of this book would not be complete without a word of praise for the publishers and their associates. They have produced a book of high quality, attractively bound and with the pages opening flat, at a modest price.

Prior to the opening chapter, which is devoted to information on the subject of natural grafting and its bearing on artificial methods, there is a glossary of terms used. There are also notes on the reasons for grafting, all of which are of value and interest, particularly to the student.

In Chapter 2 the author discusses compatibility and cambium contact, and the reader is left in no doubt regarding their importance. The following chapters deal with the role of rootstocks and their propagation. There is also excellent information on the collection and treatment of the wood or growths to be used as scions and, to emphasize the importance of the various points, each is dealt with under a separate heading.

Chapter 5 is devoted to "Tools and Accessories", and here the author covers very fully the various knives and other small tools required for the many methods of grafting that he describes. There are also useful notes on the various commodities that are necessary for the completion of the work. This is information that is so often neglected in many books dealing with the practical aspect, while for the student it provides information that is difficult to obtain.

Chapter 6 deals with the many methods of grafting, divided into two main divisions, namely, approach grafting and detached scion grafting. The reader is introduced to each method with clear and concise notes that are supported by excellent line drawings by the author and, in some instances, photographs as well. The way in which this important part of the subject is covered can be judged from the fact that some eighty pages are devoted to this chapter—nearly one-third of the book.

There is much useful information in Chapter 7, which deals with tree-raising in nurseries, and the methods adopted for grafting under glass and in the open are described and commented on. In the next chapter, Mr. Garner deals fully with the methods of grafting used to rejuvenate old trees and to change varieties. There is also information and some excellent illustrations of the methods of grafting employed to repair and save trees that have their bark girdled by animals or damaged in other ways.

The author concludes with a chapter which deals with the misuse of grafting and the interaction of stock and scion. Also discussed are those interesting if not very useful bigeneric trees known as graft-hybrids or chimeras in which an intermixture of tissues occurs to provide in growth a mixture of both genera, as, for example, *Mespilus* and *Crataegus* in *Crataegomespilus*.

A well-prepared index is provided and completes a book that should find a place on the bookshelf of all gardeners and nurserymen, as well as that of the keen amateur.

S. A. Pearce

UPPER DEVONIAN SPIRIFERS OF THE CATSKILL DELTA

"Spirifer disjunctus"

Its Evolution and Paleoecology in the Catskill Delta. By Hugo Greiner. (Peabody Museum of Natural History, Yale University, Bulletin No. 11.) Pp. iv+75+13 plates. (New Haven, Conn.: Peabody Museum of Natural History, Yale University, 1957.) n.p.

From a study of numerous specimens of Upper Devonian spirifers (Brachiopoda) from the Catskill delta of New York State, the author claims that what were formerly considered to be varieties of a single species actually constitute a tribe of genetically related species of *Cyrtospirifer*, each having a limited stratigraphic range and belonging to two principal phyletic lines.

The specimens were obtained from littoral or sublittoral beds, mainly sandstones and shales, 2,500 ft. thick, accumulated during 5–6 million years, and ranging from the base of the Chemung to the base of the Mississippian.

Hemmed in by a shore line to the east and by deeper water deposits to the west, the Catskill delta in Devonian times supported some 1,178 species, only a small number of which were near-shore dwellers like *Cyrtospirifer*. The shifting of the delta westwards resulted in sudden changes of facies and the necessity for adaptation of the tribe to various environmental niches.

Six species occur predominantly in sandstone, nine species in shale and three species are found in both shale and sandstone. Most of the species have short ranges, but two showed great adaptability to changing environment and cut across formational boundaries with no marked morphological change, both giving rise to a number of species. The ancestor of the tribe is not known; some species seem to have originated locally while others are migrants from another region, and hybrids are recognized. Early in the evolution of the group there was a considerable number of species probably associated with a narrow sublittoral zone. A broader platform with fewer ecological niches tended to produce fewer species in the later history of the region.

Attenuate forms appear earliest, but alate forms tend to occur in shaly facies and more quadrate forms in a sandy facies, though this is not consistent. Auriculation or mucronation would keep shells on the surface of the mud and prevent currents from upsetting them. The largest shells appeared relatively late.

Lateral costae number about 50 in some early forms, but later forms have about 24 broader costae, while bifurcation of costae within the sinus tends to decrease in the later species.

Small size of adductor scars are said to be indicative of weak muscles which would be suited to quiet muddy sea-floor conditions, while large adductors, coarse costae and thickened ventral umbones distinguish specimens which lived in sandy wave-swept places. The angle of divergence and length of the dental lamellae seem to be variable characters.

As a palæoecological and evolutionary study the paper is of considerable interest, but the identification of the eighteen species (thirteen of them new), some with overlapping ranges and with considerable variation in shell outline, is likely to cause trouble for the taxonomist. No statistical study of the species was attempted.

The paper is well presented, except for a number of misprints, and is illustrated by thirteen plates of excellent photographs.

It is regretted that the author could not have made a rapid survey of European species of *Cyrtospirifer*, and especially *C. verneuili* (Murchison), the type species from the Upper Devonian, Frasnian of Ferques, Boulonnais, which closely resembles some of the Catskill species in form, ornament and spinose micro-ornament. The retention of the name *Spirifer disjunctus* J. de C. Sowerby for the tribe is unfortunate, since this species is doubtfully synonymous with *C. verneuili*, and has actually been assigned to a separate subgenus. H. M. Muir-Wood

NAMES AND CIPHERS IN ORGANIC CHEMISTRY

Nomenclature of Organic Chemistry, 1957

(International Union of Pure and Applied Chemistry.) Pp. v+92. (London: Butterworths Scientific Publications, 1958.) 15*s*.

A Proposed International Chemical Notation

Prepared by the Commission on Codification, Ciphering, and Punched Card Techniques of the International Union of Pure and Applied Chemistry. Tentative version subject to revision. Pp. vii+165. (London: Longmans, Green and Co., Ltd., 1958.) 35*s*.

The already embarrassing problems of nomenclature are intensifying through the rapid acceleration of discovery in organic chemistry, resulting in the preparation of more and more complex synthetic compounds and the elucidation of the structures of natural products, often exceedingly complex. The discoverers of necessity invent trivial names, but these convey nothing to the uninitiated. The ideal name for a compound is one which will immediately tell a chemist its structure, enabling him to write down a formula or construct a molecular model. It should also be internationally acceptable, printable and suitable for indexing. There is a natural tendency for a group of workers in a new field to invent a special nomenclature in that field which may or may not be compatible with that in other fields—the steroid field is an example. A vested interest is thus created, and the unfortunate people charged with the task of standardizing meet a dilemma. Editors can do something to discourage this growth of rogue nomenclature by giving advice to authors, as they frequently do, but they may be too late.

In the two books under review we have an opportunity of comparing two entirely different systems of recording and communicating the constitution of any organic compound. The first book accomplishes a great task in revising and standardizing conventional nomenclature in limited fields; the second throws convention to the winds and makes an entirely fresh start, using little that is familiar except the initials of most of the elements.

Serious attempts to obtain international agreement on organic nomenclature date from the Geneva meeting of 1892. The next important development was in 1930, when the Liège rules were drawn up by the Commission of the International Union of Chemistry. A major revision of these rules is now being undertaken, sponsored by the International Union of Pure and Applied Chemistry and in the first book under review we see the first results of this important work. The definitive rules now recommended concern the naming of hydrocarbons of all classes, of heterocyclic systems and of steroids; that is to say, they are concerned with molecular frameworks without substituents, but including derived radicals. Hydrocarbons are divided into classes, aliphatic, monocyclic, fused polycyclic, bridged, spiro and ring assemblies, with a special group for terpenes. In the last group, many trivial names are admitted, with some changes, camphane, for example, becoming bornane. A large list of trivial names is also approved for hydrocarbons of the fused aromatic type, including such newcomers as coronene and ovalene (but not zephrene, I notice). The form biphenyl is adopted for the hydrocarbon which has always been called diphenyl in Great Britain. The systematic naming and numbering of cyclic hydrocarbons of all kinds and of heterocyclic systems follow the conventions of Patterson and Capell's 'Ring Index', so far as I could tell after a careful comparison. In addition, the useful *a* method of naming heterocyclic fused ring systems as aza, oxa, thia derivatives of a homocyclic parent is given as an alternative to the fusion system. In the field of steroids the Commission has bowed to established custom and accepted the numbering of the cyclopentaphenanthrene system, which flouts all the rules. To simplify nomenclature in this field the use of a number of trivial names is proposed, starting with 5α- and 5β-gonane for the two important stereochemical isomers of perhydrocyclopentaphenanthrene. The volume concludes with some tentative suggestions for nomenclature in the vitamin B_{12} field. The typographical conventions and spellings used in this book are those of *Chemical Abstracts*, which differ appreciably from British usage and the hope is expressed that each nation will attempt to reduce such variations as exist in their publications. In this connexion, the Chemical Society (London) has just announced its intention of making certain changes which will, incidentally, bring its usage more into conformity with American practice. In this review these changes have been adopted.

The ingenious system of ciphering developed in the second book under review is obviously the outcome of careful study. It is based on ideas put forward in 1946 by Dr. G. M. Dyson. Other people at about the same time and later were thinking along similar lines and some of their ideas have been incorporated in the final draft, though essentially it is the Dyson system. The aim is to give an unambiguous cipher to any structure without using any names, trivial or other. This would cut out linguistic difficulties and avoid the strain of having to memorize a multitude of trivial names.

A cipher is composed of letters, figures and punctuation signs. The basic idea is that any structure is made up of chains, rings and functional groups which can be represented by simple signs. A chain of n carbon atoms can be represented by C_n; a saturated ring of n carbons by An; a ring of n carbons having the maximum number of non-cumulative double bounds by Bn; all free valencies are considered to be saturated, so H need not be ciphered except in special cases. The system of numbering enables junctions, fusions and substituents to be accurately ciphered and it is to be noted that Dyson numbering of familiar rings differs greatly from conventional numbering. It is impossible here to go further into detail but a few examples may be given. Thus, C_4 is *n*-butane; C_4.C,2 is isopentane; C_4.E,1,3 is 1,3-butadiene (E represents a double bond, attached to the first and third carbon of butane); C_2.Q is ethyl alcohol (Q is oxygen, to avoid confusion with zero); B6_2 is naphthalene (two benzene rings, B6, fused); B6ZN is pyridine (Z indicates substitution, in this case of one C in benzene by N). Such examples are simple, but complexities soon arise in ciphering structures containing several rings, bridged rings, mixed assemblages of rings and chains and so on, and new rules and conventions have to be devised for these. Among the wonderful ciphers quoted is that for oxytocin, a complex polypetptide, which contains (I counted them) 179 signs and symbols, including full stops and commas, each of which is significant. Deciphering comes to resemble working out a jigsaw puzzle since, with a cipher starting with a number of rings, one has for some time no idea how these are going to be connected in the final structure. Nevertheless, it has been shown that ciphering can be done and the ciphers printed (proof correcting must be a nightmare).

The questions arise, when and how are the ciphers to be used? A few suggestions are made, for example, to use them for differentiating compounds in the major divisions of a formula index. No doubt Dr. Dyson and his colleagues are studying this aspect and will eventually publish their detailed proposals. Ciphering and deciphering will probably be a specialized task in libraries and information centres. The summit of achievement would be an electronic brain to relieve human effort.

E. H. RODD

NEW BIOCHEMISTRY

Annual Review of Biochemistry

Vol. 27. Edited by J. Murray Luck, in association with Frank W. Allen and Gordon Mackinney. Pp. vii+775. (Palo Alto, Calif.: Annual Reviews, Inc., 1958.) 7 dollars.

PROBLEMS that arise from the spate of scientific literature in the world, and in particular in biochemistry, are very real; but at the present time no comprehensive treatment of the problem can be foreseen. Nevertheless the volumes of "Annual Reviews" which appear each year make a sturdy attempt to make a real contribution to the solution of the problem of the digestion of knowledge. As biochemistry draws its pabulum from an ever-widening field of activity the efforts of a reviewer are attended by increasing frustration. The "Annual Review of Biochemistry" is the oldest of the "Annual Reviews" published in California. This twenty-seventh annual volume manages to fashion the torrent of publications in nearly twenty different aspects of the subject into some sort of smooth-flowing stream. Clearly it is not possible to please all the readers all the time, and the specialist can always find material to criticize; but there can be no doubt whatever that the "Annual Review of Biochemistry" is of the greatest importance to biochemists all over the world.

In the present volume, apart from chapters dealing with vitamins, hormones, and the metabolism of protein, fat, and nucleic acids, there are sections concerned with the "Biochemistry of Viruses" (G. Schramm), "Biochemistry of Cancer" (H. E. Skipper and L. L. Bennett, jun.), "Chemistry and Biochemistry of Antibiotics" (E. B. Chain), "Biochemistry of Fishes" (H. L. A. Tarr), "Metabolic Antagonists" (W. Shrive and C. G. Skinner), "Enzymatic Metabolism of Drugs and other Foreign Compounds" (B. B. Brodie, J. R. Gillette, and B. N. La Du). J. A. Stekol again reviews "Biochemistry in the U.S.S.R.".

There is a prefatory chapter, entitled "Impressions of an Organic Chemist in Biochemistry" by Hans T. Clarke, in which the importance of chemistry as a background to biochemistry is particularly emphasized. As an illustration of this thesis one can refer to the review of "Proteolytic Enzymes" by G. H. Dixon, Hans Neurath, and J.-F. Pechère in this volume, which has the conciseness and clarity that one expects from Dr. Neurath and his colleagues. The fact that one is now able to illustrate the activation of trypsinogen and chymotrypsinogen in terms of chemical structures, and can formulate processes which occur at the active centre of proteolytic enzymes by reactions of a chemical type, well illustrates the advances in this aspect of biochemistry. On the other hand, the discussion of "Newer Developments in Relation to Protein Biosynthesis" by H. Chantrenne is one that is at the heart of the dynamic aspects of biochemistry and as yet contains little that can be formulated in purely chemical terms. At heart a biological subject, biochemistry can snatch from the rapidly moving stream of life, systems, bits of tissue, organelles and subcellular particles of all sorts which in their behaviour seem initially to be far from the sort of chemistry that can be discussed in terms of known processes. But the biochemist reduces to manageable proportions the number of the uncontrolled features of the system, and although the processes which ultimately emerge for analysis may be complex they can be treated in terms of chemical reactions. To many, however, the most exciting part of the line of development lies in the early stages. But whichever stage of development is the primary interest of the reader, he will find much to take his attention in this volume of the "Annual Review of Biochemistry".

F. G. YOUNG

FURTHER ADVANCES IN ENZYMOLOGY

Advances in Enzymology and Related Subjects of Biochemistry

Vol. 20. Edited by F. F. Nord. Pp. vii+488. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1958.) 12.50 dollars.

ANOTHER excellent volume of "Advances in Enzymology" contains articles by biochemists from Australia, the United States, Britain, the U.S.S.R., The Netherlands, Sweden and Switzerland; fourteen enzymes are reviewed in some detail, and a number of general topics are also discussed.

There are two reviews on single enzymes by workers who have been personally responsible for much of the recent research described: by Prof. H. Theorell on "Liver Alcohol Dehydrogenase", and by Dr. A. Gottschalk on "Neuraminidase". The first describes some recent kinetic studies, particularly those using fluorimetry, a technique which is critically discussed, and relates them to the picture of alcohol dehydrogenase mechanism developed earlier by Prof. Theorell in collaboration with Dr. B. Chance. The second review is particularly devoted to the chemistry of the substrates concerned, sialic acids.

Prof. H. M. Kalckar discusses the enzymes involved in the metabolism of uridinediphosphogalactose, and the function of this compound in animals and bacteria. Drs. Vischer and Wettstein list the enormous range of transformations of steroids carried out by micro-organisms; few of these have yet been associated with isolated enzymes, and it is clear that this will be a fruitful field for the enzymologist. Drs. Deuel and Stutz discuss pectic substances and their breakdown, the emphasis being placed on the chemistry of the substrates rather than the enzymes.

A particularly important review is that of Prof. E. C. Slater on "The Constitution of the Respiratory Chain in Animal Tissues". There is still a great deal of uncertainty about several parts of the oxidation chains in animal mitochondria, and the more controversial points are clearly and persuasively discussed. Powerful arguments are urged, for example, against the view that cytochrome *b* is not involved in succinate oxidation, and against the participation of vitamins E and K in the main coenzyme-linked chain. The nature of the cytochrome reductase reaction and the function of the other cytochromes are further topics dealt with in detail; the importance of cytochrome c_1 is emphasized.

Two articles deal with the mechanism of enzyme action. Drs. Davies and Green give a clear and concise account of recent work on the mechanism of cholinesterase, especially that stemming from studies on the inhibition of the enzyme by diisopropyl fluorophosphonate. They conclude that a great deal remains to be done, particularly in explaining the differences between individual enzymes sensitive to diisopropyl fluorophosphonate which appear to have considerable similarities in amino-acid sequence at the active centre. This article may be usefully read with that of Drs. Barnard and Stein, who discuss the role of histidine in the active centres of enzymes. The chemistry of imidazole derivatives is described in detail, and the article will be of use to the many enzymologists who speculate on these matters.

Much has been written in recent years from the enzymic point of view about mitochondria and other structures in animal cells, but less has been written about plant sub-cellular structures. The gap is well filled by an account by Prof. Sissakian of the "Enzymology of the Plastids". Many enzyme systems besides those directly concerned with photosynthesis have been detected in chloroplasts, and these enzymic results are highly significant when considering the function of these bodies.

A more metabolic topic is dealt with by Dr. Kretovich, who discusses the importance of glutamine and asparagine in the nitrogen metabolism of the plant, in protein synthesis and so on. Prof. Werner Kuhn, in an article entitled "Optical Activity and Aging", develops his earlier ideas on asymmetric synthesis and loss of optical purity. Finally, the usual article on some topic on the fringe of enzymology is by Drs. Tanner and Beesch on the interesting results so far obtained by the use of antibiotics such as streptomycin in the control of plant diseases.

All in all, the volume will provide good reading for any biochemist for many a long winter's evening.

EDWIN C. WEBB

RADIOACTIVE ELEMENTS

Chemistry of the Rare Radioelements

Polonium-Actinium. By Dr. K. W. Bagnall. Pp. x + 177 + 5 plates. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1957.) 30*s*.; 5 dollars.

Uranium and Thorium

By L. Grainger. Pp. viii + 204 + 8 plates. (London: George Newnes, Ltd., 1958.) 25*s*. net.

"CHEMISTRY of the Rare Radioelements" is a specialized book which describes the chemistry of the elements polonium to actinium. It is of interest to note that, of these elements, only radium could be obtained in a pure state and in weighable amounts prior to 1939. At the present time, however, more is known about the chemistry of polonium than any of the others. This is in no small part due to the extensive programme of work carried out by the author during the past few years at Harwell. He is well qualified to write this book, and the standard he has set is surprisingly high considering the meagre amount of reliable published work on which he had to rely.

The author points out that our knowledge of the chemistry of polonium is approaching in extent that of tellurium, its lower homologue in the Periodic Table. This is largely due to the development of new microchemical techniques for handling polonium—and it should be remembered that this still usually represents work with sub-milligram amounts of the element. There are two short chapters devoted to the handling of polonium and radium and actinium. While these are useful, it would have been preferable to confine them in one chapter in which health problems and micro-radiochemical techniques were discussed in somewhat more detail.

About half the book is devoted to an exhaustive treatment of the chemistry of polonium, and this is a valuable contribution to all inorganic chemists. It is to be hoped that more work, of similar calibre, will be published on actinium. Thus, while milligram quantities of actinium metal have been prepared, most of the solution chemistry is based on tracer scale work, and this can be notoriously misleading. A reason for the small amount of work with actinium is, of course, the difficulty in estimating the isotope actinium-227, because of its weak β, and complicating decay chain. It is surprising the author has not described the use of the α-counting method, which, although requiring a good counter and a pulse analyser, is quantitative and reliable.

This is a valuable reference book and is recommended to all who are interested in the rarer elements.

As the author points out in the preface, "Uranium and Thorium" is intended to provide a reasonably comprehensive picture of the technology of uranium and thorium. It is not intended for the specialist in the metallurgical problems of nuclear power, but it does provide a good background for other scientists and engineers who are either directly concerned with the production of nuclear power or who are just interested in knowing more about uranium and thorium.

The book is, broadly speaking, divided into three parts. The first gives a good account of the occurrence, ore-processing methods and metal production of both uranium and thorium. Then the chemical and more particularly the physical properties of both metals and their compounds are discussed. The last two chapters give a short account of the use of uranium and thorium as nuclear fuels and current trends in fuel-element design in each of the countries interested in nuclear power reactors.

The subject-matter is largely drawn from the proceedings of the 1955 Geneva Conference. Although there has now been a second conference (1958), the book is still surprisingly up to date, and in a second edition it is the chapters dealing with fuel elements which will require more extensive revision. There is also an increasing amount of work being carried out on uranium alloys, for example, with zirconium, molybdenum and silicon, but these receive only a mention. The physical properties of such systems are of interest to the physical metallurgist, and their applications are of special interest to the nuclear technologist. This is a subject which might well merit a chapter to itself.

The author, who at the time this book was written was chief metallurgist to the Industrial Group of the United Kingdom Atomic Energy Authority (he is now chief metallurgist at Harwell), is well qualified to produce such an authoritative account. The book, which is reasonably priced, is strongly recommended to all those interested in the use of uranium and thorium in nuclear power production.

G. R. Hall

SATELLITE RESEARCH

Scientific Uses of Earth Satellites

Edited by James A. Van Allen. Second, revised edition. Pp. x+316. (Ann Arbor, Michigan: University of Michigan Press; London: Chapman and Hall, Ltd., 1958.) 75*s*. net.

THIS book contains an account of experiments which were proposed for the American satellite programme to be carried out mainly during the International Geophysical Year. The various chapters are based upon papers presented at a meeting of the Upper Atmosphere Rocket Research Panel in 1956 by a number of experts in the field of planetary physics. In the first edition, now almost two years old, the experiments were presented as proposals, no satellites having been launched at the time, but since then several of those suggested have been successfully carried out, and others are upon the point of being tried. The second edition now under review, coming so soon after the first, could scarcely be expected to give an account of the results so far obtained, and in fact no new material has been added. Some of the thirty-three chapters have, however, been revised and brought up to date, although this has not altered the total number of pages in the book (316). Revisions may be found in Chapter 1, where, for example, equation 42, p. 9 (which gives the motion of the line of the apsides of a satellite orbit) and the sentence following it, have been corrected. A short addendum has been made to Chapter 24, and in Chapter 33 the discussion of electron accretion by an interplanetary dust particle has been rewritten. There are other changes of a similar nature throughout the book.

The real value of the book, which must be judged to be considerable for those working in the various fields covered, lies in the basic nature of the treatment of each subject. Chapters 1, 5 and 11 discuss in some detail satellite orbits with perturbations due to the Earth's oblateness and atmospheric drag. Further perturbations arising from time and latitude variations of air density and from winds are perhaps too scantily treated to satisfy those interested in the behaviour of the recent *Sputniks* and their rockets. The visibility of satellites and optical tracking problems are the subjects of Chapters 2, 3 and 4, although no detailed mention is made of systems now in use. Satellite instrumentation is covered in a general way in Chapters 6 and 7, power sources being given considerable attention, and particular experiments for the study of the density and pressure of the Earth's atmosphere from a satellite, namely, by an accelerometer recording drag on an orbiting inflated sphere and by an ion gauge of special design, are detailed in Chapters 10 and 12.

The study of the meteorology of the Earth by observing tropospheric weather systems as revealed by clouds is proposed in Chapter 13. The method involves scanning the Earth by narrow-angle photoelectric detectors in a spinning satellite, the detector outputs being telemetered to a chain of ground stations. Chapter 14 describes a method whereby it should be possible to obtain the temperature of the atmosphere as a function of the optical depth by observation of the thermal radiation from the Earth and its atmosphere in the far infra-red.

Four chapters are devoted to investigations in the ultra-violet, which include continuous monitoring of the Lyman alpha-emission from the Sun, observations of the resonance radiation at 1216 A. arising from sunlit hydrogen atoms in interplanetary space, and a prediction of the appearance of the sky in the ultra-violet based upon the study of ultra-violet stellar magnitudes. (No mention is made in the latter of the recent discovery of hitherto unsuspected ultra-violet emitting objects.)

Chapters 20, 21 and 22 are concerned with cosmic rays and auroral radiations. It is here again that a suggestion that the second edition might be somewhat premature could arise, owing to the absence of a discussion of the extremely important Van Allen radiation belt discovered by an American satellite vehicle.

The four succeeding chapters describe proposed geomagnetic measurements of the main field and atmospheric current systems, Chapters 23 and 24 being particularly extensive. Instrumentation is given in some detail, and the importance of establishing the presence or absence of an extra-terrestrial ring current is naturally stressed.

Ionospheric studies occupy five chapters, mainly from the aspect of propagation experiments. Chapter 28 briefly describes possible temperature and electron density measurements using a Langmuir probe.

Chapter 32 reviews work on the acoustic detection of meteoric particles, already carried out using rockets, and recommends the technique for satellites. An alternative meteor detector based on the erosion of resistive elements on the outside surface of a satellite is briefly described in Chapter 8. Interplanetary dust is further discussed in Chapter 33, particular attention being paid to the motion of charged dust particles near the Earth.

Each chapter includes a list of references, in general very extensive, but there is no index. Diagrams are clearly reproduced, and chapter sections and sub-headings well displayed.

E. B. Armstrong

Science and Religion in Seventeenth-Century England

By Prof. Richard S. Westfall. (Yale Historical Publications, Miscellany 67.) Pp. ix+235. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1958.) 36s. net.

IN view of its importance as a landmark in human history, it is not surprising that the seventeenth century is receiving special attention from both historian and scientist. The present book is not merely one of many, it has a distinct approach of its own; indeed, the publishers claim that it "is the first attempt to study systematically the religious opinions of seventeenth-century scientists in the light of their importance to the future of Christianity". As the word "virtuoso" constantly occurs, Prof. Westfall wisely explains that he uses it to describe "one who has a general interest in arts and sciences, or who pursues special investigations in one or more of these; the meaning is further restricted to those interested specifically in natural science". The term appears in the title, the "Christian Virtuoso", published by Boyle in 1690.

The book under review contains many illustrations from the writings of the virtuosi on such subjects as the harmony of science and religion; the harmony of existence; Divine Providence and natural law; the growth of natural religion; reason and faith. Among the familiar names specially mentioned are Robert Boyle, Nehemiah Grew, John Locke, John Ray and Edmond Halley. It is fitting that the concluding chapter of Prof. Westfall's work should be headed "Isaac Newton: A Summation". It begins with an extract of Newton's letter to Richard Bentley, dated December 10, 1692: "When I wrote my treatise about our system, I had an eye upon such principles as might work with considering men for the belief of a deity; and nothing can rejoice me more than to find it useful for that purpose". There are references also in this chapter to Newton's theological writings, and a discussion of his views in relation to those of the other virtuosi.

The inclusion of a "Bibliographical Essay" of some ten pages enhances the value of Prof. Westfall's book, and invites further study of an outstanding period in science, religion and philosophy.

H. D. ANTHONY

Le Système du Monde

Histoire des Doctrines Cosmologiques de Platon à Copernic, Tome 8. Par Prof. Pierre Duhem. Pp. 512. (Paris: Hermann, 1958.) 3,400 francs.

THE posthumous publication of Vols. 6–10 of Pierre Duhem's monumental work "Le Système du Monde" has now proceeded to the eighth volume, being the second of a group of three which is devoted to the physics of the Parisian school in the fourteenth century. The first two chapters (8 and 9) deal with the problems of the vacuum: its possibility, the so-called *horror vacui* of Nature, the movement of bodies *in vacuo*. In the next two chapters (10 and 11) the movement of falling and projected bodies is treated. This is a most important subject in medieval physics, as it contains the germ of modern dynamics. Then the treatment turns to cosmology again: the application of the ideas of the Terminists on celestial motions is discussed and the various attitudes of medieval thinkers towards astrology are reviewed. As was remarked in the review of the preceding volume, we owe a debt of deep gratitude to the editors for the fact that the great work that Duhem left unfinished at his death in 1916 is none the less being completed. In the meantime, however, the study of medieval science has been pursued and our ideas on the subject have notably progressed. It is no longer possible to consider Duhem's statements and opinions as final, as we all were inclined to do when the first volumes of "Le Système du Monde" appeared in the years 1914–17. Nowadays no reader striving after a knowledge of medieval science which is abreast of the time can afford to neglect studying the works of A. Maier. This, however, necessitates some important modifications in Duhem's exposition.

This does not detract from the pleasure of reading him. His style is an admirable specimen of French elegance and clarity from which it is no detraction that some corrections are necessary in the text.

E. J. DIJKSTERHUIS

Benedict de Spinoza

The Elements of His Philosophy. By Prof. H. F. Hallett. Pp. xvi+171. (London: The Athlone Press, University of London, 1957. Distributed by Constable and Co., Ltd.) 25s. net.

THIS is a compact, scholastic exposition of Spinoza's philosophy, the result of profound reflexion on the original texts. There is no evaluative discussion of Spinoza's ideas; Prof. H. F. Hallett has tried to speak only with his master's voice. His book provides a remarkable example of sympathetic understanding, in attitude and intellect, of a lapsed mode of thought, and it will unquestionably be illuminating for the expert in studies of Spinoza—and for those who thought they were experts. But I fear that to the rest the book will remain closed not long after it is opened. The author's scholastic style expresses itself continually in sentences such as, "A perfect primordial being possesses all potency in eternal act; but an imperfect and privative being possesses only the potency that it actualizes, though, as privative, potency is durationally available to it that is not *by it* durationally actualized" (p. 6), which might well discover truths to the initiated but can only baffle the novice for whom the book is confessedly designed. Again, the background to Spinoza's thinking, the patterns and pressures that moulded his mind and the materials that he transformed in his own peculiar way are neither elucidated nor referred to; and the principal scholarly work (by Wolfson) which provides this very background is nowhere mentioned, not even in the bibliographical note. Thus my reaction to Prof. Hallett's mature and careful presentation is one of respect and admiration, mixed with regret at his stylized obscurity and at the absence of historical enlightenment.

PETER NIDDITCH

ESP and Personality Patterns

By Gertrude Raffel Schmeidler and R. A. McConnell. Pp. xiii+136. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1958.) 25s. net.

SOME years ago, at the City College, New York, Dr. Schmeidler discovered that if she asked her experimental subjects whether or not they believed in the possibility of extra-sensory perception (ESP), their subsequent scores showed that the believers' average score was significantly above mean chance expectation, whereas the unbelievers tended to score at chance-level or slightly below. She labelled these two groups the 'sheep' and the 'goats', respectively. Later experiments have amply confirmed this original finding, and it is one of the not very large number of facts in experimental parapsychology that can be regarded as established.

This fact is interesting, since it is not only an addition to the evidence as to the reality of extrasensory perception, but also an indication that there are personality differences correlated with ESP ability It leads to many further questions, some of which are further explored in this book; many of which are indicated but not yet answered. The obvious further question as to a more exact specification of the personality correlates of ESP ability has been tackled mainly with the help of the Rorschach test. Since, however, this test is known to have low reliability, no very certain evidence as to the answer has been obtained or is likely to be obtainable by this means. The suggestion by the authors, that some of the diversity in findings of different investigators of this topic may be due to personality differences between investigators, is an important speculation that awaits experimental verification.

The experimental work of Dr. Schmeidler has until now been scattered in the technical journals. In collecting it in one volume and in obtaining the collaboration of Dr. McConnell (particularly for a needed strengthening on the statistical side), she has done the student of parapsychology a considerable service. The result of this collaboration is an interesting and authoritative account of an important piece of research. R. H. Thouless

The Black Fens

By A. K. Astbury. Pp. xi+217+55 plates. (Cambridge: The Golden Head Press, Ltd., 1958. Distributed in Great Britain and Eire by W. Heffer and Sons, Ltd.) 42*s*.

THIS excellent book is likely to appeal most to the layman interested in finding out more about one of the most distinctive regions of Britain, but also has much of interest to geographers. The first part of the book is concerned with the origins and physical characteristics of the black peats, which since the beginnings of major drainage schemes in the seventeenth century have come to provide Fenland farmers with exceptionally productive soils. But agriculture in the Fens faces a unique combination of hazards. There can be few areas in the world where, within the span of one year, a farmer may have to contend with his soil being flooded in winter and actually catching fire in summer. Since draining, the peat has shrunk many feet while the silt river beds have maintained their original height. These processes make control of surface-water progressively more difficult and the consequences of a failure of flood protection measures more serious. The problems of farming, and of building roads, railways and houses upon the spongy peat are illustrated with a wealth of detail that obviously springs from a long and intimate acquaintance with the area. Particularly to be commended is the use of carefully selected aerial photographs printed opposite sketch maps of the area covered by them, which serve to show the great importance of the "roddhams". These silt beds of ancient water-courses provide the only stable sites for building in the peat region.

In the second part of the book the question of the origin of the Fen waterways is examined. It is remarkable how little is known about most of these ancient channels. After an exhaustive study of many of them, based on considerable field work, the author puts forward a good case for believing that many of them were constructed by the Romans, but rightly points out the difficulty of proving this or any other hypothesis.

The book is well served by many good photographs and sketch maps and a large folding map which shows nearly all the places mentioned in the text. M. A. Morgan

Bone and Radiostrontium

By Arne Engström, Rolf Björnerstedt, Carl-Johan Clemedson and Arne Nelson. Pp. 139. (New York: John Wiley and Sons, Inc.; Stockholm: Almqvist and Wiksell; London: Chapman and Hall, Ltd., 1957.) 70*s*. net.

ANY information concerning the metabolism of strontium-90 must be welcomed at the present time and the authors have presented a valuable account of work carried out in their own laboratories. One chapter is devoted to a discussion of the distribution of mineral salts in bone in which the techniques of microradiography and microinterferometry are fully described. In another chapter the authors discuss the nature of bone salts and the structure of bone tissue, particularly with reference to the ability of the apatite crystals to attract various types of ions by surface adsorption. A calculation of the radiation dose from beta-rays within a plane parallel sandwich of radioactive trabecular bone and inactive bone marrow is described in great detail. It is a pity that the authors did not also include calculations using cylindrical geometry, which might be more applicable in the case of another concentration site of strontium-90, namely, Haversian systems.

In the discussion summarized at the end of the book, the authors deduce a value, 0·1 μc., for the maximum permissible burden of strontium-90 in human beings. Since this is 10 per cent of the value recommended by the International Commission on Radiological Protection for occupationally exposed persons, the authors' arguments have been carefully examined. The radiation dose within a microscopic tissue element in bone contaminated with the radioisotope has been discussed in relation to an assumed cancer dose of 1,000 r. of external radiation. There is, however, no discussion about the importance of the relationship between dose or dose-rate and the incidence of cancer, or of the importance of the volume of tissue irradiated. A comparison between a body burden of 0·1 μc. strontium-90 and an unspecified burden of radium known to produce malignancies is, of course, valueless. There is in any event no comment about the effect of alpha- and beta-particle range on the non-uniformity of radiation-dose or about the relative biological effectiveness of the two radiations. A second calculation assumes that a dose of 10 r. to a microscopic site in bone marrow will produce detectable blood changes. In the absence of a more detailed discussion on the type of blood damage expected, on the dose-response relationship and on the effect of varying the time over which the dose is given, this discussion is also without value.

It is unfortunate, therefore, that the authors, who obviously have a valuable contribution to make in this field, did not make a more careful survey of the present position before attempting to suggest a new level for the maximum permissible burden of strontium-90. J. Vennart

Lebensgemeinschaften der Landtiere

Ihre Erforschung unter Besonderer Berücksichtigung der Zoozönologischen Arbeitsmethoden. Von Dr. Janos Balogh. Zweite verbesserte und erweiterte ausgabe des 1953 erschienenen werkes "Grundzüge der Zoozönologie". Pp. ii+560. (Budapest: Akdemiai Kiado, 1958.) n.p.

THE Budapest school of terrestrial biology is well known for its work on the ecology of the soil fauna. Dr. J. Balogh's book is of value because it introduces this important work to a wider audience, but it is perhaps of even greater significance as a synthesis of theory and of methods of analysis current in the different world schools of community ecology.

The first edition of this book was a stimulating and thoughtful analysis of animal synecology, logically beginning with definitions of the community (biozonose) and later departures from earlier concepts, followed by an analysis of the community, its detection and delimitation, its structure and subdivision, its inorganic and living content, spatial and temporal changes, the food chain and production biology and finally a consideration of schemes of analysis and study in practical use. The new edition has been extended so that it is now an up-to-date and cosmopolitan account of this field. To this have now been added sections which provide the most extensive review now in print of methods for the collection, examination, culture and extraction of terrestrial invertebrates, supplemented by sections on vertebrates by Turček and on agricultural land faunas by Heydemann (of Kiel). Although statistical aspects of sampling are not considered, no one who already works in this field can fail to find some useful details of technique which will be new to him, and no one entering the field could be referred to a more complete résumé of methods. A. MACFADYEN

The Dawn of Life

By Dr. J. H. Rush. Pp. 258. (London: English Universities Press, Ltd., 1958.) 15s. net.

DR. J. H. RUSH has made a brave attempt to present a comprehensive account of the origins of living matter in terms intelligible to those without much knowledge of physics and chemistry. He has a rare skill for interpretation, and is adept both at choosing the right word and in using a suitable figure of speech for illuminating his text. Yet it is doubtful if his book can be called more than a gallant failure. Although the grand strategy is clear and well-conceived, the tactics are scarcely suitable to achieve the objective.

Besides descriptions of the hypothetical beginnings of the universe and the earth, the author includes accounts of the physico-chemical origin of living things, theories of evolution, life on other planets and the emergence of mind. All this, supported by the relevant laws of physics and a description of chemical theory, does not make for easy reading even for those with some knowledge of chemistry and physics. Like so many books intended for the general reader, the author has attempted too much in too short a space. If the first three chapters had been expanded and written with the intelligent secondary modern schoolboy in mind, Rush might well have produced an outstanding popular scientific work. He is to be congratulated for this attempt, and should be encouraged to write other popular works with the belief that sometimes greater clarification is achieved more by omission than commission. T. H. HAWKINS

An Introduction to Tropical Agriculture

By Sir Harold Tempany and D. H. Grist. Pp. xvi+347+12 plates. (London and New York: Longmans, Green and Co., Ltd., 1958.) 40s. net.

THE late Sir Harold Tempany has attempted "to provide a logical and coherent account of the background to agriculture in the tropics", which his co-author believes "should be of great value to students, agricultural officers and administrators" in these areas. Sir Harold, who had had a wide experience of tropical agriculture, died before completing his task, which was then entrusted to Mr. D. H. Grist. With the increasing demand for tropical agricultural products and the urgent need to improve methods of land use and production and thereby raise the living standards of many tropical peoples, such a book should be very welcome, particularly as no such account had been published for some years. Unfortunately, the volume under review does not reach a standard adequate to meet this need.

The book is very uneven in content. Much space is wasted in explaining simple facts which are more adequately dealt with in the numerous elementary text-books on temperate agriculture. Thus a whole chapter is devoted to fertilizers in which the role of the major elements in plant nutrition and the nature of the common fertilizers are explained, while shifting cultivation, the most important system of farming in the tropics, with its wide range of variation and modern modifications, is dismissed in one page. The treatment of many subjects is so generalized, uncritical and superficial that it provides little information of practical value and some of it is inaccurate. It is possible to quote many statements of the obvious which might well have been omitted, such as "irregularities in the amount and incidence of rainfall cause great difficulties and these naturally increase as the drier regions are approached", which appears in almost identical words no less than three times in two consecutive pages. J. W. PURSEGLOVE

Flora of Manitoba

By H. J. Scoggan. (National Museum of Canada Bulletin, No. 140.) Pp. v+619. (Ottawa: Queen's Printer, 1957.) 5 dollars.

THE province of Manitoba is larger than the United Kingdom and is centrally placed in Canada both physically and botanically, but by a trick of fate it had remained uncovered by the three great manuals dealing with the flora of temperate North America. This neglect is now remedied by the excellent book under review. The major vegetation types of Manitoba are prairie (now mostly under cultivation), swamp and dry sandy forest near the Great Lakes, boreal forest, tundra forest and arctic tundra in the extreme north-east. These are briefly described, with their climates, and are illustrated by photographs. The rest of the book, apart from a bibliography, tabular classifications of species and lists of additions and exclusions, is the Flora proper, which follows many conventional lines.

There are no descriptions of individual taxa, and critical taxonomic comment is cut to the minimum, but the specific keys seem unusually ample and satisfactory, and there are many references to recent generic revisions. Careful notes are given on habitat and on distribution both within and outside the area, the "first report" of each taxon is always cited and so too, usually, are the "earliest collection seen" and the northernmost collection. Hybrids are omitted:

otherwise, there would surely be some mention of this proclivity among the 28 species of *Salix*. 1,417 species of vascular plants, including 193 introductions, are found in Manitoba, the largest families being the Cyperaceae (159 native species), Compositae (144) and Gramineae (114). No less than 118 species of *Carex* are listed, but there is no genus comparable, at any rate in treatment, to the British *Rubus* and *Hieracium*. The author is to be congratulated on a valuable piece of work which will reward the close scrutiny of British and European botanists concerned with the preparation of Floras. N. Y. SANDWITH

Diseases of Domestic Animals in New Zealand

Prepared by the Technical Committee, N.Z. Veterinary Association, Inc. Pp. x+240. (Wellington: Editorial Services, Ltd., 1958.) 35*s*.

THIS book is not for the arm-chair reader but for the busy veterinary surgeon needing some form of reference to which he can turn for essential and up-to-date factual information. It deals with the significant diseases of domesticated animals and poultry, only as they occur in New Zealand, grouped under the headings, bacterial, viral, protozoal, fungal, parasitic, nutritional and metabolic, those caused by poisons, and miscellaneous. Under each heading, the diseases are listed alphabetically, and each disease is covered in one or, at most, two pages in précis form through the use of subheadings, for example, species affected, notifiable, distribution, occurrence, herd incidence, etiology, mode of infection, signs, pathology, diagnostic aid, prognosis, treatment, etc. The brevity of style and standard form of presentation have been used deliberately for ease of reference, so that one is presented with an accurate and authoritative summary of the disease position in New Zealand. Some minor criticisms could be made. As one example, it is a little distracting to find that all the intestinal nematodes of a particular host animal are treated as causing one disease. Such criticism, however, is trifling and amply compensated by the wealth of information presented so simply and concisely and with so few errors. There is an index of eight pages which could, with advantage, have contained more entries such as helminths, cestodes, trichostrongyles or even worms, to mention a few. The eight appendixes listed in the contents table were not included in the reviewer's copy. J. N. OLDHAM

Birds of Cyprus

By Dr. David A. Bannerman and W. Mary Bannerman. Pp. lxix+384+31 plates. (Edinburgh and London: Oliver and Boyd, Ltd., 1958.) 63*s*. net.

ONE has come to expect volumes from Dr. Bannerman that are sumptuous as well as scholarly, and here he and his wife present another. The scale may even seem luxurious for the avifauna of so small a territory, but Cyprus has a considerable ornithological literature and its bird-life shows interesting features. The island lies on the fringe of the tremendous migrations of the Levant, and more than half its 333 recorded species are purely birds of passage; others are winter visitors. Some 70 species breed, a third of them as summer visitors: among the residents, 14 belong to races peculiar to the island. It is remarkable that, in spite of extensive forests, there are no woodpeckers and no nuthatch.

There are references to birds going back to the fourteenth (falconry only) and sixteenth centuries; serious ornithological publications date from 1787 onwards; in the past few years ornithologists in the Armed Forces have added numerous records; the Bannermans themselves spent some months on the island in 1954 and in 1957–58 for the purposes of the book, and they have drawn both on the other sources and on their own observations. For the benefit of the student in Cyprus, there are notes on identification (with numerous figures) and on extra-limital distribution: Greek and Turkish names of species are given. For ornithologists elsewhere, the information about local status is of importance as a contribution to a wider pattern. The illustrations include some fine colour plates by D. M. Reid-Henry and Roland Green. LANDSBOROUGH THOMSON

British Fermentation Industries

By J. M. Whitmarsh. Pp. xiv+133. (London: Sir Isaac Pitman and Sons, Ltd., 1958.) 25*s*. net.

THIS condensed account of industrial fermentations, which is restricted to British practice, embraces both old and new processes, but deliberately excludes consideration of the potable and antibiotic industries. The manufacture of industrial alcohol, acetone and butanol, lactic acid, vinegar, baker's yeast, citric acid and of sorbose is described as illustrative of the older processes. The inclusion of the obsolescent industrial alcohol and acetone-butanol processes, both of which have been superseded by synthetic chemical processes, is justifiable in that they have provided, over a number of years, fundamental knowledge and technological experience which has facilitated the rapid large-scale development of newer processes. It is especially valuable to have good condensed accounts of these new, less-familiar, processes as exemplified by those by which vitamin B_{12}, riboflavin and dextran are manufactured and by which difficult steroid transformations may be effected; for it is in these fields, as well as in that of antibiotic production, that the fermentation industries may be expected to continue to develop and prosper. In all, Dr. Whitmarsh has written a very useful account of the subject within his self-imposed restrictions. Despite compression, there is adequate technical detail to provide a good introduction to the fermentation industries for new entrants, of whom the biochemical engineer should be particularly mentioned. There are few errors of fact or of typography, but the taxonomically minded will boggle at reading that *Euglena* is a mould (p. 82) and that *Rhizopus nigricans* is a *Mucor* species (p. 115).

Textbook of Biochemistry

By Prof. Benjamin Harrow and Prof. Abraham Mazur. Seventh edition. Pp. ix+557. (Philadelphia and London: W. B. Saunders Company, 1958.) 52*s*. 6*d*.

PROF. Benjamin Harrow has a long and honourable career as a writer of text-books of biochemistry. In 1935 he and Carl P. Sherwin collaborated as joint editors of a "Text-book of Biochemistry" to which chapters were contributed by a number of authorities. This book set a standard of clarity and breadth of information which was upheld later by a text-book with Prof. Harrow as the sole author, of which editions have already appeared ranging from the first in 1938 to the sixth in 1954. For the sixth edition Prof. Harrow was joined by Prof. Abraham Mazur as joint author, and now a seventh edition is called for, as might be expected, four years after the sixth.

Since the rate at which biochemistry develops continues alarmingly, each edition of a general text-book needs substantial revision, and the new edition of this standard work has been widely revised. In particular, the chapters on nucleoproteins and the various phases of intermediary metabolism have been rewritten, and the previous one on photosynthesis replaced by sections in the chapters on carbohydrate chemistry and on carbohydrate metabolism. It is a reflexion of the coherence of growing knowledge that changes of this sort now are almost inevitable. The former two chapters on digestion and adsorption have been incorporated into one, while that with the title "Detoxication" has been quite properly replaced by one called "Metabolism of Organic Chemicals".

With the immense growth of knowledge of which account is taken it is surprising, but welcome, that this edition should be a little smaller than the previous one. The pages of text, numbering more than 500, are still eminently readable, and although some sections naturally are less up to date than others, on the whole the authors keep surprisingly well abreast of current knowledge. They are to be congratulated on maintaining a standard text-book in such a uniformly good state. F. G. YOUNG

General Biochemistry

By Prof. Joseph S. Fruton and Prof. Sofia Simmonds. Second edition. Pp. xii+1077. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 144*s*. net.

THIS book gives a very complete and readable account of the chemistry, physical chemistry and intermediate metabolism of the important chemical constituents of the living organism. The chemical chapters on proteins are extensive and provide a most detailed and informed survey. A chapter on elementary thermodynamics with a useful introduction to the second law and the concept of free energy is also included.

The whole of the subject-matter is introduced and developed as an experimental science, and sufficient experimental details are given for a proper appreciation of the theoretical discussions and generalizations. In many cases the experimental methods are described and explained in some detail, and this is especially true of the more recent methods of chromatography and isotopic tracer techniques.

All the usual metabolic sequences and interconversions of biological syntheses and degradation are ably discussed, and generally the most recent views and enzymic steps are included. These metabolic surveys are mainly concerned with animal biochemistry, although there is a very good chapter on photosynthesis by green plants.

The book is thus an excellent and comprehensive introduction to the subject, and since it is well documented it may well serve for a few years as a reference book to some parts of biochemistry. However, as a text-book for use by students in Great Britain it has two disadvantages. One of these is its very high price and the other is the level at which it is written. For use in most elementary courses the book is too detailed, especially for those students who do not wish to specialize in the subject; while the advanced student, although finding the book very useful, must have access to the many adequate reviews and whenever possible direct reference to the important original papers. D. H. NORTHCOTE

Metals and Enzyme Activity

Biochemical Society Symposium No. 15 held at the University of Leeds on 13 July 1956. Organized and edited by E. M. Crook. Pp. v+102. (Cambridge: At the University Press, 1958.) 21*s*. net cloth bound; 15*s*. net paper bound.

IN the Biochemical Society symposium held at the University of Leeds, in 1956, inorganic chemists and biochemists joined in discussing aspects of the functions of metals in enzyme systems. This book contains the papers that were presented at that meeting, together with the discussions which followed.

The symposium opened with a short introductory paper by R. S. Nyholm describing recent work on metal ligand bonds, a topic which was developed further in a paper by L. E. Orgel on the solution chemistry and structural chemistry of some metals important in enzyme activity. Some suggestions on the mode of action of metals in the catalytic hydrolysis of peptide bonds were made by B. R. Rabin, who gave a short account of conflicting views on the nature of the enzyme-metal-substrate complex. Later in the session, F. C. Happold and R. B. Beechey considered the univalent metal ions as non-specific activators of enzymes and attempted to explain their function. The role of metals in metallo-flavoproteins was summarized by F. Bergel and B. C. Bray, who discussed the involvement of the metals in electron-transfer reactions. The symposium ended with a paper by E. C. Slater describing briefly and conveniently the classification and properties of the cytochromes.

This meeting of chemists and biochemists has made a valuable contribution to this fascinating problem, and it is unfortunate that more than two years have passed before the papers appeared in print. O. T. G. JONES

Electronic Theory and Chemical Reactions

An Elementary Treatment. By R. W. Stott. Fourth edition. Pp. viii+112. (London and New York: Longmans, Green and Co., Ltd., 1958.) 12*s*. net.

THE author was one of the first to attempt a simplified account of the theories of reaction mechanism and his success may be measured by the fact that this is a fourth edition of a book which first appeared a little more than fifteen years ago. This edition retains the very simple treatment which characterized the earlier editions, together with additions and emendations. The bibliography which accompanies each chapter has also been extended and is now, in some cases, of considerable proportions.

The content of any book is largely a matter for the author, and his success in this case suggests that he caters very satisfactorily for his intended readers. Nevertheless, I feel that some change of balance in the material might be made in a future edition. There is, for example, no discussion of hydrogen-bonding, while about four pages are devoted to a demonstration of the equivalence of the hydrogen atoms in benzene. This latter, formal demonstration might be curtailed or even eliminated by mentioning the Raman and infra-red spectral evidence that this molecule is planar and centro-symmetrical. The X-ray evidence upon hexamethylbenzene, or benzene itself, may be quoted instead. Inclusion of the former topic would do much to remove the difficulty that not all covalently bonded compounds are of a high volatility, 100 per cent sulphuric acid being a particular example.

A few minor errors have also appeared in the text. Thus, the omission of a negative charge from the extruded group X^- in the bimolecular substitution process on p. 53, the reference to a diagram as on p. 65 which is really on p. 67, the possible confusion which may arise (p. 85) by describing Cl^- as a chlorine ion instead of the established chloride, the more so as possibly a Cl^+ is involved in this reaction, and finally, the reference p. 62 should be to Braude and not Brande.

The book is well and pleasingly produced and adequately indexed. One can confidently look forward to the appearance of a further edition within the near future. R. I. Reed

Fundamentals of Optics

By Prof. Francis A. Jenkins and Prof. Harvey E. White. Third edition. Pp. vii+637. (London: McGraw-Hill Publishing Company, Ltd., 1957.) 64*s*.

In its third edition, this excellent text-book has been largely rewritten to include recent developments in both experiment and theory, and to bring the treatment into line with modern ideas on the teaching of the subject. There can be few books ranging from the detailed drawing-board computations of ray-tracing, and the analytical discussion of third- and fifth-order aberration, to the scintillation counter and its possible use to examine simple interference experiments in the light of the uncertainty principle. The mathematical proofs of formulae have been presented more concisely, and the complex-quantity notation used in the wave-theory section of the book makes for easier reading. The diagrams, many of which illustrate graphically the physical meaning of an analytical expression, are really helpful in supplementing the mathematics. The book is well produced, and can be recommended as very good value. G. R. Noakes

Nuclear Magnetic Resonance

Annals of the New York Academy of Sciences, Vol. 70, Article 4. By H. S. Gutowsky and seventeen other authors. Pp. 763–930. (New York: New York Academy of Sciences, 1958.)

A conference on nuclear magnetic resonance was held by the New York Academy of Sciences in November, 1957, and the papers presented at this meeting have now been published. The papers are concerned with some of the more recent applications of nuclear magnetic resonance to chemical problems. The first part deals with the fundamental interactions which determine the nuclear resonance line-widths and shapes, their chemical shifts and multiplicities. The origins of these interactions are summarized by C. P. Slichter, and H. S. Gutowsky gives an excellent review of the chemical interpretation of chemical shifts and spin – spin coupling constants and of the principles of the analysis of the sometimes complex high-resolution spectra. This is followed by a description by Schneider, Bernstein and Pople of the detailed analysis of the very complex spectra of pyridine and its deuterium derivatives. The study of hindered internal rotation in organic molecules is discussed by W. D. Phillips, and of chemical exchange kinetics by W. G. Schneider and L. W. Reeves. P. C. Lauterbur describes experiments to explore the use of the spectra obtained from carbon-13 nuclei in natural abundance in organic compounds. The use of high-resolution nuclear resonance spectra to study really complex organic molecules is illustrated by F. C. Nachod and by M. Saunders and A. Wishnia. The complementary use of nuclear magnetic resonance and infra-red spectra is discussed by H. Finegold with especial reference to the chemistry of organic compounds of phosphorus, and R. B. Williams gives a detailed and authoritative discussion of the conditions necessary for the use of nuclear magnetic resonance for quantitative analysis.

For the reader with some acquaintance with the subject of radio-frequency spectroscopy, this collection of papers provides an excellent survey of the uses of the method in chemistry. R. E. Richards

The Preparation of Programs for an Electronic Digital Computer

By Dr. Maurice V. Wilkes, Dr. David J. Wheeler and Dr. Stanley Gill. Second edition. (Addison-Wesley Mathematical Series.) Pp. xiv+238. (Reading, Mass.: Addison-Wesley Publishing Company, Inc.; London: Academic Books, Ltd., 1957.) 60*s*.

This is a second and enlarged edition of the book first published in 1951. As before, the main emphasis is on the preparation of programmes for *Edsac* I together with the specification and detailed coding of selected library sub-routines. Additional material has been added, however, on machines possessing different order codes and different input and output systems, while twelve pages are devoted to automatic programming and the concept of 'floating addresses'.

The book is in three parts, its basic plan following that of the first edition. Part 1 gives all the information required to prepare a programme for the *Edsac* and deals in general terms with other machines. Part 2 specifies the most important of the *Edsac* library sub-routines and Part 3 gives the complete list of instructions for selected sub-routines.

The book will be of most value to the beginner who wishes to learn some of the principles underlying programming. In particular those intending to programme *Edsac* I will welcome the revised description of the order code, in which important changes have occurred since the publication of the first edition. These include the provision of a *B*-register, the unconditional jump order and output on to punched paper tape.

The use of the machine is clarified by a number of simple examples, and exercises—many with specimen solutions provided—are set to enable the reader to test his understanding of the machine.

The book has a more attractive layout than previously, and the authors are to be commended on this revised edition. E. L. Albasiny

Fourier Transforms and X-ray Diffraction

By Prof. H. Lipson and Dr. C. A. Taylor. Pp. vii+76. (London: G. Bell and Sons, Ltd., 1958.) 18*s*. 6*d*. net.

This is a well-prepared book at a comparatively moderate price, suitable for third-year undergraduates and junior postgraduates, but containing much that will interest senior research workers and university teachers. When the theory of X-ray diffraction by crystals is approached by way of the Bragg relation, the transition to the reciprocal lattice can often seem highly artificial, and the idea of the molecular transform may never be reached at all, especially by the non-mathematically inclined. The authors argue convincingly that if what is interesting is the content of one unit cell, then it is more logical and may be more fruitful to begin with the transform and examine its modification by the crystal lattice. The means of doing this optically, which is a subject of which they have special experience, is only briefly mentioned in an appendix, and is to be dealt with in a further publication. Applications of the Fourier transform theory to the trial-and-error method, to sign determination, to the direct recognition of molecular features, to structural imperfection such as stacking disorder, to the effects of crystal size and shape and other problems are given brief but stimulating consideration. In dealing with temperature effects, however, the impression is given that the diffuse regions around all reciprocal lattice points are similar and parallel, and this is an error which should be corrected in the next edition.

Kathleen Lonsdale

Introduction to Difference Equations with Illustrative Examples from Economics, Psychology and Sociology

By Prof. Samuel Goldberg. Pp. xii+260. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 54s. net.

In recent years new developments in the social sciences, economics, psychology and sociology have involved an increasing use of mathematics, and a branch of the subject which has found widespread application is the theory of difference equations. The book under review covers this topic and is "primarily intended for social scientists". The exposition is at an elementary level, and the style is sufficiently easy for the ordinary undergraduate to understand the methods for solving difference equations and to learn of some of the recent research applications such as inventory analysis and probability models for learning.

Two features of the book deserve special mention. There are a number of worked-out examples to illustrate the text and more than 250 problems with answers, so that the work should be very useful as a text-book. There are also many references to recent research papers, where the research student may find more detail. Altogether the book gives the impression of having been carefully written and with the student very much in the mind of the author.

Some topics of a relatively advanced nature are gently introduced towards the end. These include matrix methods, generating functions, a characteristic-value problem and the analysis of equilibrium and stability. The latter, unfortunately, is only discussed in the case of a second-order auxiliary equation, and the reviewer believes that it would have been useful to discuss the case of higher-order equations, via the Routh-Hurwitz determinantal conditions.

L. S. Goddard

An Introduction to Combinatorial Analysis

By John Riordan. (A Wiley Publication in Mathematical Statistics.) Pp. xi+244. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 68*s*. net.

The classical text-book by Netto, "Lehrbuch der Combinatorik", published in 1901, is unknown to most present-day mathematicians; and the subject-matter, namely, problems of enumeration, has been generally out of favour for two decades or more. Now the book under review appears and new life is thereby injected into the subject. The author has given a careful exposition of various developments of recent decades which have until now remained locked away in scattered journals and proceedings. Perhaps the most valuable aspect of the present work is this bringing together of material and the connected account of a topic which is important in various branches of applied mathematics and probability theory, as well as in certain parts of pure mathematics where there is still an interest in finding 'the number of ways'.

For the contents an introductory chapter on permutations and combinations is followed by an important chapter on generating functions, including the polynomials of E. T. Bell. Then there are chapters on the principle of inclusion and exclusion, cycles of permutations, distributions and occupancy. The next chapter, which comes near to parts of graph theory, is concerned with partitions, compositions, trees and networks. The explicit results find application in the theory of electrical networks and in systems engineering, including coding problems in data transmission. The last two chapters cover permutations with restricted position.

The book includes a large number of problems and explicit results at the end of each chapter. These are for the serious student who wishes to know 'how to do it' rather than what has been done. They are, as the author says, "put in a form to aid rather than baffle", and they assume, as does the text itself, a considerable degree of mathematical maturity on the part of the reader.

L. S. Goddard

Technology of Instrumentation

By Prof. Eric B. Pearson. (Applied Physics Guides.) Pp. 202. (London: English Universities Press, Ltd., 1958.) 25*s*. net.

Instruments are indispenable in modern scientific and engineering work, and an understanding of the principles of operation is essential if correct results are to be obtained. The main emphasis is on the performance of the standard laboratory milliammeter type of instrument. The static and dynamic characteristics of instruments are explained and the importance of a knowledge of the transient response of an instrument is demonstrated. Electronic instruments are not included, and it is unfortunate that the cathode-ray oscilloscope is omitted since it is valuable where non-sinusoidal wave-forms are to be measured.

The application of instruments to control systems occupies the larger part of the book. The principles of servomechanisms are dealt with at length, and topics discussed include velocity feedback, reduction of velocity lag and general conditions for stability. A chapter on servomechanism components describes a number of elements used for measuring the difference in angular position of output and input shafts of a mechanism. This is followed by a description of electronic and hydraulic amplifiers and motors for supplying power to an output shaft. The final chapter on instrumentation of mathematics describes a number of electrical and mechanical devices for integrating and multiplying.

The book forms a useful introduction for students in the subjects of instrumentation and servomechanisms, but it is unfortunate that the author has not considered a wider range of measuring instruments and measurement principles.

R. L. Grimsdale

(*Continued from p.* 950)

Ano-dorsal fin formula. Adult specimens collected by Frost in Kenya have shown that this character cannot be used alone to distinguish between even adult *A. n. labiata* and *A. mossambica*, although *A. b. bicolor*, the 'short-finned eel', is immediately recognizable by this method and is not represented in the present material. Figures for this character are given in Table 1.

Vertebral counts. In both the Tana and the Sabaki specimens the vertebral counts are rather low. Thus Barnard[6] considers 100–105 normal for *A. mossambica*, and Frost (*in litt.*) 107–115 for *A. n. labiata*. But even with X-ray photographs, such counts are difficult in the smaller specimens and an error of two or perhaps three vertebræ is possible.

The eighteen Tana River elvers have been referred to *A. n. labiata* and the single Sabaki River elver is considered to be *A. mossambica*, the first true elver to be recorded in Kenya. There is no doubt from the abundance of adults in the river at certain times of the year that elver and post-elver stages must migrate upstream in considerable numbers, and further observations at the Merilla Barrage and the construction of an elver trap on the Ragati River (Tana system) at our Inland Fishery Research Station should reveal much of interest.

We are grateful to Dr. W. E. Frost for additional adult measurements and for helpful comment on these observations, and we are especially indebted to Dr. Geoffrey Kelham, of Nairobi, for some strikingly successful X-ray photographs of these difficult small subjects.

VERNON D. VAN SOMEREN
PETER J. P. WHITEHEAD

Fish Division (Research),
Ministry of Forest Development,
Game and Fisheries,
Nairobi, Kenya. Dec. 5.

[1] Frost, W. E., Colonial Office Fish. Pub., No. 6 (1955).

[2] Harrison, A. C., *Piscator*, **9**, 19 (1955).

[3] Skead, C. J., *Piscator*, **10**, 28 (1956).

[4] Jubb, R. A., *Nature*, **180**, 47 (1957).

[5] Frost, W. E., *Nature*, **179**, 594 (1957).

[6] Barnard, K. H., *Piscator*, **7**, 8 (1953).

'Bat Erosion' at Niah Great Caves

AT the Great Caves of Niah, Sarawak, West Borneo[1], there is a relatively soft coral limestone of Miocene date in which these vertical cavities are common, and as in Trinidad[2], found where there are no stalactites. On the other hand, the rock in these places is damp and there may often be a ring of very slowly forming drips around the mouth of a cavity. Moreover, only small family groups of *Miniopterus witkampi* regularly use these sites as roosts, rarely more than five at once, hanging in a bunch from the top-dead-centre[3]. It is doubtful whether the scrabbling action of these small bats could ever excavate such cavities, and indeed the remarkable symmetry and the vertical axis of each formation suggests that it is due to solution rather than the activity of bats.

Nevertheless, at least two species of bat at Niah are responsible for erosion of different sorts in the cave. The small *Hipposideros galeritus* (a roundleaf horse-shoe bat) roosts singly and there are certain spots on the cave wall where a bat may be found every day. Here the action of the bats' claws keeps a small area of the surface rough and free from the slimy coating that covers it elsewhere in the deep interior. This roughened patch is often slightly concave, perhaps worn by mechanical erosion.

More positive is the effect of the huge, densely massed colony of *Cheiromeles torquatus* (the naked bat), which occupies a large gallery at one of the highest points of the roof. Fragments of rock quite often fall from this site and are deeply eroded and heavily stained with the bats' excrement. Presumably chemical action weakens the limestone until it breaks under its own weight or under the burden of a *Cheiromeles*, which weighs about six ounces.

Examination of the bat-remains recovered at mid-palæolithic levels in the 1958 Niah dig prove the presence of both *H. galeritus* and *Cheiromeles* at levels corresponding to an age of well over 40,000 years[4], as well as other bats no longer found in the cave[5]; so that, if occupation has been continuous, both these species have had plenty of time to leave their mark.

TOM HARRISSON

Sarawak Museum,
Kuching.

MEDWAY

Department of Anatomy,
University of Birmingham.
Jan. 13.

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Galeal Structure in Adult Mosquitoes

IN a previous communication[1], studies of the finer structure of the galeæ in adult mosquitoes were reported. It was pointed out that the galea formed the functional maxilla and typically consisted of a strengthening chitinous rod with a fine outer lamella the tip of which carried a number of variously shaped teeth. Further studies, ranging over eight genera of mosquitoes of the Ethiopian region, have revealed that although there is a variety of morphological types, a progressive reduction in the outer lamella is evident. It should be noted that generic and specific differences in the mouth parts of adult mosquitoes have only been poorly investigated[2], and early studies described only general morphological differences in the trophi, usually of species of known medical and veterinary importance[3-5]. In the present studies, freshly killed mosquitoes were used whenever possible and the heads were soaked in 5 per cent potassium hydroxide for 48 hr. After this they were transferred to a slide, the trophi teased apart with a fine steel point and mounted in polyvinyl alcohol. General examination was carried out at ×100 and detailed examination at ×450.

It has been found that there are four main types of galeal structure which are shown diagrammatically in Fig. 1. Type *A* has a well-developed outer lamella with the distal portion expanded and typically small teeth without pointed tips. Type *B*, which has a simple blade-like appearance, is the commonest form found and the teeth are subject to wide variation in both form and number although the greater proportion are elongate with pointed tips which extend beyond the outer margin of the lamella. Type *C* has the terminal region of the lamella reduced, but this is

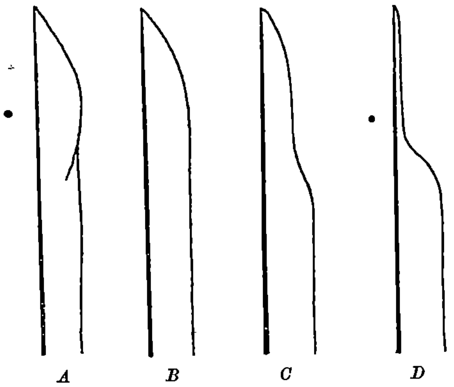

Fig. 1. Diagrammatic representations of the four types of galeal structure as described in the text, showing the progressive reduction of the terminal region of the outer lamella. The teeth typically carried on the lamella are not shown

never less than half the width of the main portion of the lamella. The teeth vary in size and form, but most project beyond the margin of the lamella. Type *D* has the terminal part of the lamella further reduced and in all observed cases this was less than half the width of the main portion. In the majority of cases the teeth were seen to project beyond the margin of the lamella. The species possessing these four types of galeal structure are shown in Table 1.

Table 1. SPECIES POSSESSING THE TYPES OF GALEAL STRUCTURE AS DESCRIBED AND FIGURED

Type *A*: *Uranotaenia balfouri*, *U. annulata*, *Aedes simpsoni*.

Type *B*: *Anopheles gambiae*, *A. demicolus*. *Hodgesia nigeriae*, *Uranotaenia bilineata*, *Mansonia metallicus*, *M. annetti*, *M. africanus*, *M. uniformis*, *Eretmapodites semisimplices*, *Aedes longipalpis*, *A. apicoargenteus*, *A. stokesi*, *A. simulans*, *A. dendrophilus*, *A. irritans*, *Culex horridus*, *C. fatigans*, *C. decens*, *C. annulioris*, *C. cinerellus*.

Type *C*: *Anopheles coustani*, *A. rufipes*, *A. pharoensis*, *Uranotaenia ornata*, *U. philonuxia*, *U. caliginosa*, *Aedes aegypti*, *A. africanus*, *A. pseudoafricanus*, *A. luteocephalus*, *Culex duttoni*.

Type *D*: *Ficalbia hispida*, *Eretmapodites chrysogaster*, *Aedes circumluteolus*, *A. argenteoventralis*, *Culex tigripes*, *C. albiventris*, *C. nebulosus*.

It is difficult at this stage to establish any satisfactory relationship between the galeal structure and the feeding habits of the species. The genus best represented in this study, *Aedes* Mg., possesses each type of galea but nearly all the species represented are known to be anthropophilic in some degree. It must not be overlooked, however, that genera do exist which are capable of biting but have not been observed to do so, while most species take blood for the purpose of ovarian maturation[6]. Thus it would seem that there exists a series of galeal forms represented by the successive reduction of the terminal region of the outer lamella which is not related to feeding method. In the previous communication already mentioned particular attention was paid to the finer structure of the outer lamella and in these present studies further observations have been made upon it. In the great majority of species examined the outer lamella has been seen to have a particulate nature, the individual portions being at right angles to the chitinous rod or directed slightly posteriorly. Early workers[7] stated that this lamella was divided into separate areas by transverse lines which in some cases produced indentations of the outer edge, while it has also been recorded that this structure was essentially membranous with only fine and sometimes anastomosing striations. The present observations tend to support the former view, although the particulate nature was noticeably absent in most *Aedimorphus* species.

Finally, mention must be made of the teeth attached to the galeal lamella. The maxillary index (the average number of teeth on the two maxillæ) has been shown to be related to the power to infect in anopheline mosquitoes[9] and has also been used for demonstrating different races in mosquitoes of the same species but bred from different habitats[10,11]. On the other hand, it was also established that the maxillary index of adults bred from the same egg batch was subject to a wide variation[12]. In the present studies the variations in the number of teeth is considerable, but due to insufficient data concerning feeding habits it is not possible at this stage to construct any well-defined relationship between this activity and maxillary index.

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Antimicrobial Substances from Resistant and Non-resistant Seeds

WHY certain plant varieties are resistant to plant pathogenic micro-organisms while others are not resistant is not understood. It is possible that resistant plants produce more antibacterial and antifungal substances than non-resistant plants in order to protect themselves against microbial invasion. This idea was advanced by Irving, Fontaine and Doolittle[1] and was tested by Little and Grubaugh[2]. The latter investigators used the expressed juices of several resistant and non-resistant common garden plants and tested them against both plant and animal pathogenic micro-organisms. They concluded that no distinction could be drawn between the activities of the juices of resistant and non-resistant plants. Similar results were reported by Tims[3]. It was thought advisable to investigate seeds in an attempt to demonstrate any difference between resistant and non-resistant plants. Furthermore, the solvents used in the preparation of seed extracts was not only water but also di-ethyl ether, acetone, ethyl alcohol (95 per cent) and *n*-butyl alcohol. The use of organic solvents for removing antimicrobial substances from plants is the more common procedure[4,5].

The media used for growing the bacteria was a nutrient agar and broth, while the fungi were cultivated in Sabauraud's dextrose agar and broth. The following seven test organisms were employed: *Serratia marcescens*, *Escherichia coli*, *Staphylococcus aureus*, *Mycobacterium smegmatis*, *Candida albicans*, *Erwinia caratovora*, and *Streptomyces venezuelae*. Five additional plant pathogenic micro-organisms were also tested against some of the seed extracts. All bacterial cultures were incubated at 37° C. for 24 hr.

Table 1. ANTIMICROBIAL ACTIVITY OF RESISTANT AND NON-RESISTANT CABBAGE SEEDS

Seeds	Zones of inhibition (mm.)							
	E. coli	*S. aureus*	*S. marcescens*	*S. smegmatis*	*C. albicans*	*E. caratovora*	*S. venezuelae*	*F. oxysporum* f. *conglutinans*
Jersey Queen*								
Water extract	7	2	6·5	2	4·5	11	10	1
Diethyl ether extract	5·5	7·5	2	9	4	5	9	7·5
Acetone extract	6	8	2	9	6·5	5	10	4·5
Ethyl alcohol extract	5·5	8·5	0	9	4·5	5	8	3·5
n-Butyl alcohol extract	2·5	6·5	0	5	0·5	2·5	5	3
Detroit*								
Water extract	7	8	2	9	2·5	7	10	1
Diethyl ether extract	5	9	3	10	6	8	9	10·5
Acetone extract	5	9	3	13	7	8	10	10
Ethyl alcohol extract	5	10	3	12	6	8	10	9
n-Butyl alcohol extract	6	9·5	2·5	12	6	6	10	9
Danish Ball Head								
Water extract	0·5	3·5	0	3	0·5	0·5	3	0
Diethyl ether extract	0	4	0	4	1	1	2·5	0
Acetone extract	0	4·5	0	5	0·5	2	3·5	0
Ethyl alcohol extract	0	1	0	1·5	0	0	1	0
n-Butyl alcohol extract	0	1	0	1	0·5	0	1	0
Penn State Ball Head								
Water extract	7	1	4	2	0	10	9·5	0
Diethyl ether extract	0	3	0	3	0	1	2	0
Acetone extract	0	0	0	0·5	0	0	0·5	0
Ethyl alcohol extract	0	1	0	0·5	0	0	0	0
n-Butyl alcohol extract	0	0	0	0	0	0	1	0

* Jersey Queen and Detroit are resistant, Danish Ball Head and Penn State Ball Head are non-resistant seeds. 0 signifies zone of inhibition absent. All zones are from disk edge to zone edge.

except *S. venezuelae* (24-hr. incubation at room temperature), *E. caratovora* and *Pseudomonas phaseolicola* (48-hr. incubation at room temperature). All the fungi were incubated at 37° C. for 3 days except the following plant pathogens which were incubated at room temperature : *Helminthosporium victoriae* strain 1 and strain 6 (4-day incubation) ; *Ustilage avenae* strain 38–1, strain 38–2, strain 38–3 (7-day incubation) ; *Colletotrichum lindemuthianum* (7-day incubation) ; and *Fusarium oxysporum* f. *conglutinans* (2-day incubation).

Extracts of all seeds were prepared as follows. 20 gm. of the dry seeds were added to 50 ml. of solvent and allowed to soak for 1 hr. The material was next macerated in a Waring blendor for 2 min., then filtered. The aqueous extracts were passed through a Seitz filter. Filter-paper disks (6·35 mm. diam.) were saturated with each extract and allowed to dry in air. The procedure was repeated so that each disk contained four applications of extract. The filter-paper disk method[6] was used for determining the presence of antimicrobial activity. In this method 1 ml. of microbial broth culture was added to approximately 10 ml. of melted agar in sterile Petri dishes and allowed to solidify. The prepared disks were then placed on the surface of the seeded agar and incubated. Measurements of zones of inhibition surrounding the disks were recorded with a millimetre ruler and an illuminated Quebec colony counter. All experiments were conducted six times.

The following varieties of bush bean (*Phaseola vulgaris*) were found to possess no activity against the seven test organisms or against *C. lindemuthianum* and *P. phaseolicola* : Contender (resistant), Tender Long (resistant), and Black Valentine (non-resistant). Pinto Bean III (resistant) and Pinto Bean Tenderpod (non-resistant) were found to exhibit the same negative results. Extracts prepared from the following varieties of oat (*Avena sativa*) : Navarro (resistant), LMHJA (resistant) and Tama (non-resistant) showed no activity against the seven test organisms or on *H. victoriae* strain 1 and 6, *U. avenae* strains 38–1, 38–2 and 38–3. Of the extracts prepared from different varieties of cantaloupe seeds (*Cucumis melo*), di-ethyl ether extracts of Delicious (resistant) and Honey Rock (non-resistant) showed slight activity on two of the seven test organisms. However, cantaloupe Honey Ball Pink Flesh (non-resistant) and cantaloupe No. 5 Powdery Mildew (resistant) showed no activity against all seven test organisms. Results with extracts from cabbage seeds (*Brassica oleracea* var. *capitata*) listed in Table 1 indicate that resistant cabbage seeds possess greater amounts of antimicrobial substances than do non-resistant seeds.

The antimicrobial substance present in cabbage plants is known as rapine[7]. It may be this organic polysulphide[8] that is present in greater amounts in resistant cabbage seeds than in the non-resistant variety. Failure to obtain any antimicrobial activity from other resistant seeds studied in this investigation cannot be explained. Perhaps the antimicrobial substances are liberated during seed germination. Studies in this field are now in progress.

We wish to thank Dr. J. S. Tidd (Asgrow Seed Growers Inc., Connecticut) for his generous supply of seeds ; Dr. L. L. Dean (University of Idaho) for bean varieties ; Dr. H. C. Murphy (Iowa State College) for oat varieties ; Dr. H. H. Luke (University of Florida) for cultures of *Helminthosporium victoriae* ; Dr. W. J. Zaumeyer (U.S. Department of Agriculture) for *Colletotrichum lindemuthianum* ; and Dr. C. S. Holton (University of Washington) for cultures of *Ustilago avenae*.

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Oxygen Deficiency and Radiation Damage in the Insect *Rhodnius*

REDUCTION in radiation damage under conditions of low oxygen tension during the exposure has been demonstrated in a number of plant and animal tissues[1]. This report deals with similar effects in the insect *Rhodnius prolixus*. Latent radiation damage in 'resting' cells of the epidermis of *Rhodnius* is expressed as a burn at delayed moulting following a blood meal[2]. In these studies, the delay in moulting and the size of the burns have been utilized as convenient indices of the oxygen effect during X-irradiation.

Unfed 4th instar nymphs were irradiated on the dorsal surface of the abdomen through a hole, 1·6 mm. diam., drilled in a lead shield 5 cm. in thickness[2]. During exposure (at 16 cm. from the target of a 2 MeV. X-ray machine ; dose-rate 6,000 r. per min. as measured in air without the shield) the insects were enclosed in a small chamber through which either air or nitrogen was circulated at a rate of 3 litres per min., after bubbling through water at room temperature. *Rhodnius* can be held in nitrogen for periods of 45 min. without injury ; however, the insects are completely immobilized after 1½ min. The nymphs were held in either air or nitrogen for 10 min. prior to irradiation. After exposure they were fed and returned to an incubator at a constant temperature of 25° C. and a relative humidity of 75 per cent.

Throughout the dose-range employed in these experiments, and for both criteria of damage, the effect inflicted by irradiation in air was two to three times that produced when the same dose was delivered in nitrogen (Fig. 1). The delay in moulting following irradiation at the lowest dose in nitrogen was barely perceptible (controls moult in 14 days), but was large after an equal dose in air. Burns did not develop after exposure in nitrogen at doses below 120 kr., but they were invariably present with doses as low as 60 kr. in air.

Thus, oxygen deficiency produces a considerable amount of protection from X-irradiation in the epidermal cell layer in *Rhodnius*. As indicated previously, and confirmed by unpublished cytological studies, the delay in moulting is due to mitotic inhibition in the epidermis prior to moulting. The inhibition of division is particularly striking in this organism because the epidermal cells enter division synchronously at a fixed time after a meal of blood. The ratio between the dose in air and the dose in nitrogen that produces equal effects is between 2·5 and 2·6, a value that agrees with those given by Evans *et al.*[3] for mitotic delay.

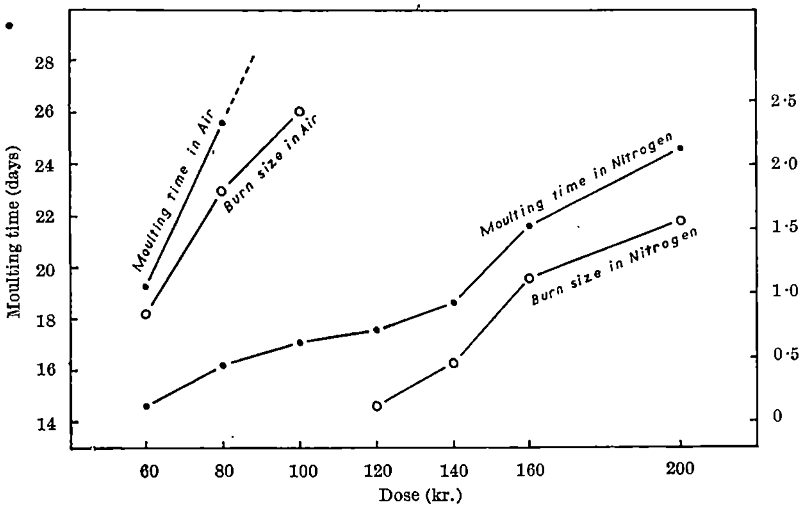

Fig. 1. Moulting times and sizes of burns of 4th instar *Rhodnius* nymphs irradiated in air and in nitrogen. Each point represents the mean from the results with five individuals. Two insects died during ecdysis after exposure to 100 kr. in air (moulting time indicated by dotted line) ; the burns were measured after death. The moulting time after feeding for unirradiated controls under similar conditions of temperature and humidity was 14 days

Further details of these experiments will be published elsewhere.

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Effects of Kinetin, Gibberellic Acid and Certain Auxins on the Development of Shoot Buds on the Protonema of *Pohlia nutans*

DURING recent investigations[1] on the effects of light of various wave-lengths on the development of the protonema and the formation of shoot buds in *Pohlia nutans* (Hedw.) Lindb., it was discovered that buds were formed only in light which included the red region of the spectrum. Furthermore, experiments on the supply of various concentrations of sucrose or glucose to the protonema suggested that the effect of red light was not merely a trophic one, but that a specific formative stimulus was probably involved. Since several authors have found that certain of the physiological responses of various flowering plants to kinetin or gibberellic acid are similar to those induced by red light, for example the expansion of leaf tissue and the onset of germination in certain dormant seeds, it seemed that it might be of interest to study the effects of these two physiologically active substances on the development of the protonema and the initiation of shoot buds in *Pohlia nutans*.

Aseptic cultures were prepared from small protonema inocula on a standard Knop's agar, with addition of various concentrations of kinetin, kinetin + 0·1 mgm./l. indoleacetic acid, gibberellic acid and, for comparison, 0·1 mgm./l. indoleacetic acid. The cultures were grown under artificial light from fluorescent tubes ('Natural') giving 375 foot candles at the level of the cultures. The temperature was regulated at 22–24° C. Another series of cultures was grown with addition of vari-

Table 1. EFFECTS OF VARIOUS GROWTH SUBSTANCES ON THE RADIAL GROWTH OF THE PROTONEMA AND ON BUD FORMATION IN *Pohlia nutans*. Mean diameter of cultures in mm.* and number of buds (*B*)† in brackets

Dates‡	Aug. 31, 1957	Sept. 10, 1957	Sept. 25, 1957	Nov. 11, 1957
Gibberellic acid				
100 mgm./l.	15	27§	38	54
10 ,,	19	35	53 (15·3 *B*)	67
1 ,,	22	35	50 (17·8 *B*)	64
0·1 ,,	22	33	50 (12·2 *B*)	64
Kinetin				
10 mgm./l.	14§	22	35	50
1 ,,	15§	24	37	47
0·1 ,,	16§	24	37	51
Kinetin (+ 0·1 mgm./l. indoleacetic acid)				
10 mgm./l.	18‖	29	41	55
1 ,,	17‖	25	36	54
0·1 ,,	17‖	27	42	56
Indoleacetic acid 0·1 mgm./l.	17	28	40 (7·8 *B*)	56
Control	19	32	49 (9·6 *B*)	67

* Mean measurements of three similar Petri dish cultures.
† Number of buds on the date when they were first observed in the cultures.
‡ Cultures started on August 14, 1957.
§ Large number of buds.
‖ Many buds.

ous concentrations of the three auxins : indoleacetic acid, naphthaleneacetic acid, and indoleacetonitrile. The results obtained with the first series of cultures are summarized in Table 1.

It will be seen from Table 1 that all the concentrations of kinetin supplied, whether with or without the addition of indoleacetic acid, resulted in the early appearance of a large number of shoot buds on the protonema ; in fact, the number formed was so great that it was both impracticable and unnecessary to carry out counts of shoot buds for comparison with bud formation on the other protonema cultures. With gibberellic acid there was a similar stimulation of bud formation at the highest concentration used (100 mgm./l.), but the three lower concentrations had relatively little effect. Neither gibberellic acid nor kinetin had any great effect on the growth of the protonema. With the three auxins tested, there was complete inhibition of bud formation in naphthaleneacetic acid at all three concentrations, 0·1, 1·0 and 10 mgm./l., in indoleacetic acid at 10 mgm./l. and in indoleacetonitrile at 50 mgm./l. A reduced number of buds was produced in indoleacetonitrile at 1 mgm./l. and at 10 mgm./l. The inhibition of bud formation in indoleacetic acid and naphthaleneacetic acid is in agreement with results obtained by previous workers[2,3]. Indoleacetonitrile had apparently not been tested previously.

The results with kinetin and gibberellic acid are of interest in that not only is the number of buds increased but also the date of their first appearance advanced as compared with the control cultures. Gorton and Eakin[4] similarly observed that kinetin increased the number of shoot buds on the protonema of *Tortella caespitosa*, but in contrast with the results reported here, they failed to obtain any earlier appearance of the buds in the presence of kinetin. We are not aware of any previous study of the effects of gibberellic acid on the development of buds on moss protonemata, although its action on the growth of the protonema has been followed in *Splachnum ampullaceum*[5].

It may be concluded from the present work that kinetin and gibberellic acid can both stimulate the formation of buds on the protonema of *Pohlia nutans*, and in this respect are similar in action to red light. It remains to be seen, however, whether these substances can promote the development of buds on a protonema which has been maintained throughout its growth in complete darkness.

We are indebted to Prof. E. Boyland, Chester Beatty Research Institute, for the supply of kinetin, and to Dr. P. W. Brian, Akers Research Laboratories, for the gibberellic acid.

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CYTOLOGY

Some Effects of Colchicine on Lampbrush Chromosomes

ISOLATED lampbrush chromosomes from the oocytes of many vertebrates have been subjected to various treatments to obtain information about the basic structure and organization of chromosomes. Lampbrush chromosomes are ideally suited for studies of this kind for they are long (350–850μ), easily isolated and can be treated without fixation and viewed immediately with an inverted phase microscope system[1,2]. This enables the experimenter to observe the action of the reagents upon the chromosomes soon after treatment and with minimum handling.

Solutions of pepsin, trypsin, ribonuclease and deoxyribonuclease have been applied to lampbrush chromosomes. Where the first three reagents destroy the material coating the lateral loops without destroying the linear integrity of the chromosomes, deoxyribonuclease effects a fragmentation of the lateral loops and of the axis of the chromosomes to which the loops are attached. Gall[3] has shown by electron microscopy that although the coating surrounding the loops is destroyed by pepsin, the loop axis remains integral and attached to the axis of the chromosome from which it originates. Callan and MacGregor[4] have demonstrated for the first time that deoxyribonuclease induces a fragmentation of the loop axis and chromosome axis, which is conclusive evidence that deoxyribonucleic acid exists not only in the main axis of the chromosome but also in the lateral loops.

Colchicine has long been known as a spindle inhibitor and mitotic poison. We have found that colchicine elicits a change in the morphology of lampbrush chromosomes in *Triturus viridescens*.

The chromosomes were isolated in a 0·59 per cent sodium chloride solution from nuclei of oocytes. The colchicine was dissolved in the same saline used for isolating the chromosomes. Colchicine was found to be effective at a concentration of 50 mgm./cm.³. Controls were run using the saline solution only. The preparations were then examined in an unfixed condition in specially constructed slides using an inverted phase-contrast microscope as proposed by

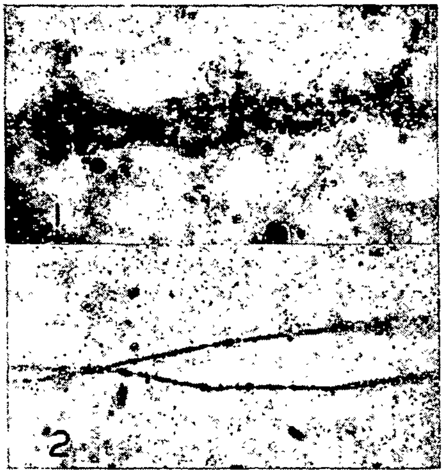

Fig. 1. Portion of an untreated bivalent fixed and stained with iron-alum hæmatoxylin showing intact loops. Fig. 2. Portion of a colchicine-treated bivalent fixed and stained with iron-alum hæmatoxylin. (× 1,000)

Gall[1]. Similar colchicine-treated and control preparations were made and fixed in formaldehyde vapour for 15 min. After fixation the slides were placed in 5 per cent formalin for 2–3 min. and stained with aceto-orcein or iron-alum hæmatoxylin. They were then placed in absolute alcohol to remove the excess stain, and the depression was filled with immersion oil and a coverslip applied to render the preparations permanent. These slides were compared with the unfixed preparations examined with the phase-contrast microscope. In both cases the results were identical.

It was found that while colchicine caused no disruption in the linear integrity of the chromosomes, there was a complete absence of loops along the entire length of the chromosomes (Figs. 2 and 4) except for the giant loops which remained. The control slides showed no absence of lateral loops (Figs. 1 and 3). Chromomeres extend along the entire axis of normal lampbrush chromosomes and render the axis cylinder of uneven diameter. In the chromosomes treated with colchicine it was noted that the axis is more uniform in diameter than in the controls and that the chromomeres are closer to one another than normally. This may be caused by a contraction of the chromosome following colchicine treatment. Most of the early experimenters with colchicine thought that the extra contraction of the chromosomes following treatment with the alkaloid drug resulted from the absence of a functioning spindle and was not an effect of a direct action on the chromosomes. However, Ostergren[5] claimed that since the extra chromosome contraction is present in prophase nuclei, it cannot be entirely due to a suppressed spindle or prolonged metaphase. This seems to be also the situation with the colchicine-treated lampbrush chromosomes for they are prophase chromosomes (diplotene).

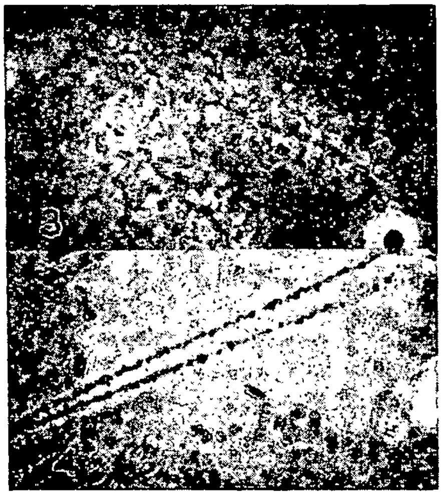

Fig. 3. Phase-contrast photograph of untreated bivalent (unfixed). Note presence of lateral loops. Fig. 4. Phase-contrast photograph of bivalent after colchicine treatment (unfixed). Note absence of lateral loops and intact axis. (× 1,000)

There are two pieces of evidence indicating that the main axis of the loop is not destroyed either along its length or at its point of origin with the axis of the chromosome. Since the interchromomeric connexions on the axis of the chromosome are not disrupted following treatment with colchicine and since there is an apparent contraction of the chromosome, it would seem that the loop axes must also contract, for they are continuous with the interchromomeric strands[3]. Also, while the loops are absent after treatment, the giant loops, when observed, are always attached to their point of origin although they do not show their usual extension into the saline; rather they appear to be drawn closer to the axis of the chromosome.

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Induction of Structural Chromosome Changes by Visible Light

It has been known since the beginning of this century that visible light is able to induce inhibitory and lethal effects on living organisms when oxygen and some sensitizing substance (which absorbs the light) are present. This phenomenon has been called 'photodynamic action'. The biological effects are believed to be due mainly to a photosensitized oxidation of organic material[1]. The fact that mutations can be induced photodynamically in micro-organisms has been shown by Döring[2] and Kaplan[3–5]. Previous studies have failed to demonstrate the production of structural changes in chromosomes among the effects induced in plant root-tips by visible light in the presence of some sensitizing substance[6,7]. The dyes used in these studies, eosin and neutral red, have no particular affinity for the cell nucleus. It seems reasonable to assume that in order to induce changes in the genetic material the light has to be absorbed by dye molecules present inside the cell nucleus. Therefore, acridine orange, which, like a number of other acridine derivatives, has a high affinity for nucleic acids[8,9], was chosen as the sensitizing substance in the present study of the effect of visible light on chromosome structure in the root-tip cells of the broad bean, *Vicia faba*.

Table 1. THE FREQUENCIES OF CHROMOSOMAL ABERRATIONS PRODUCED AT VARIOUS OXYGEN TENSIONS BY VISIBLE LIGHT IN BEAN ROOT TIPS PRETREATED WITH ACRIDINE ORANGE. ROOTS ILLUMINATED FROM ONE SIDE ONLY. *p*H OF *M*/150 BUFFER SOLUTION = 5·8

Duration of illumination (min.)	Pretreatment with acridine orange (+ or −)	Concentration of oxygen in the gas phase (per cent)	Number of metaphases analysed	Abnormal metaphases (per cent)	Aberrations/100 cells		
					I Isolocus breaks	II Exchanges	I + II
90	−	100	100	0	0	0	0
0	+	100	100	1	1	0	1
45	+	0	100	0	0	0	0
45	+	1	100	1	1	0	1
45	+	20	100	3	4	0	4
45	+	100	300	17	19	5	24
60	+	100	100	28	32	8	40

In the absence of light, concentrations of acridine orange less than 10^{-5} *M* proved to be non-toxic to the roots. In the presence of light, a strong toxic effect was obtained by concentrations of acridine orange greater than 10^{-6} *M*. This toxic effect was to a large extent eliminated by the experimental procedure finally adopted. When the bean seedlings had developed lateral roots, 0·3–1 cm. long, they were transferred to solutions of acridine orange made up of 3·5–5 × 10^{-6} *M*/l. acridine orange in tap water. In these solutions, the seedlings were allowed to grow in the absence of light for about 20 hr. Before the seedlings were exposed to light, excess dye was washed out by keeping the roots immersed in tap water for 2–3 hr. During the illumination period, the seedlings were in 'Lucite' vessels with their roots immersed in *M*/150 phosphate buffer solutions. The 'Lucite' vessels were the same as those which had been used previously in X-ray experiments. They have been described in detail elsewhere[10]. The different gas mixtures were introduced into the vessels through fritted glass filters. Oxygen-free nitrogen was obtained by passing tank nitrogen (containing 0·06 per cent oxygen) over active copper in a Meyer–Ronge column[11]. When the roots were exposed to light in the presence of a respiratory inhibitor, the seedlings were kept under anaerobic conditions for 10 min. before an oxygen-free solution of the inhibitor was introduced into the vessel. During the treatment, the desired gas or gas mixture was bubbled through the solution. The light sources were Philips 'Attralux' lamps, type 13378*E*/44, 24 V., 150 W. To prevent a marked rise of the temperature of the solution surrounding the roots, the 'Lucite' vessels were immersed in running tap water during the period of illumination. Between the source of light and the roots were 2·5 cm. air, 0·2 cm. glass, 13·5 cm. water and 1 cm. 'Lucite'. When the seedlings were illuminated from one side only, the temperature of the solution inside the 'Lucite' vessels was stable at 15° C.; when the seedlings were illuminated from two sides, the temperature varied between 15 and 18° C. In most experiments the seedings were kept, after the illumination, with their roots immersed in tap water at 20° C. in the absence of light for 22 hr. Before fixation, the roots were treated with 0·05 per cent colchicine for 4 hr. at 20° C. in the dark. The roots were fixed in alcohol–acetic acid, 3 : 1, and the slides prepared as permanent Feulgen-squashes.

Table 1 shows that structural chromosome changes can be produced by visible light in root-tips pretreated with acridine orange. However, a marked effect is obtained only when the gas bubbled through the solution contains more than 20 per cent oxygen. In the absence of either acridine orange or light, no significant effect is produced. Other experiments have shown that no aberrations seem to appear during the first 10 hr. after the treatment. In that respect, the photodynamically induced aberrations are similar to those induced by radiomimetic chemicals such as di-(2.3-epoxypropyl)ether[12], potassium cyanide[13], and tert. butylhydroperoxide[14]. In contrast to the radiomimetic chemicals mentioned, X-rays seem to be most effective in cells which enter mitosis within 8 hr. after the irradiation[12].

The induction of structural chromosome changes by visible light requires the presence of both oxygen and a sensitizing substance and appears, thus, to be a typical photodynamic effect. As a result of a photosensitized oxidation, organic peroxides may be formed.

Table 2. THE EFFECT OF 'CUPFERRON' ON THE FREQUENCIES OF CHROMOSOMAL ABERRATIONS PRODUCED BY VISIBLE LIGHT IN BEAN ROOT-TIPS IN THE PRESENCE OF ACRIDINE ORANGE. ROOTS IN EXPERIMENTS I–III ILLUMINATED FROM ONE SIDE; ROOTS IN EXPERIMENTS NOS. IV–V ILLUMINATED FROM TWO SIDES. *p*H OF *M*/150 BUFFER SOLUTION = 5·8. AFTER EACH TREATMENT, 100 CELLS WERE ANALYSED

Experiment No.	Duration of illumination (min.)	Pretreatment with acridine orange (+ or −)	Concentration of oxygen in the gas phase (per cent)	Treatment with 400 µ*M*/l. 'Cupferron' (+ or −)	Abnormal metaphases (per cent)	Aberrations/100 cells		
						I Isolocus breaks	II Exchanges	I + II
I*a*	45	+	0	+	33	33	19	52
b	45	+	1	+	30	28	8	36
c	45	+	20	+	9	7	2	9
d	45	+	100	+	21	13	6	19
II*a*	45	+	0	+	50	57	28	85
b	0	+	0	+	0	0	0	0
III*a*	45	+	0	+	44	82	42	124
b	45	+	10	+	9	5	5	10
IV*a*	30	+	0	−	0	0	0	0
b	30	−	0	+	3	3	0	3
c	0	+	0	+	5	4	1	5
d	30	+	0	+	38	39	24	63
e	30	+	1	+	40	37	26	63
V*a*	30	−	1	+	8	4	4	8
b	30	+	1	+	53	51	52	103
c	0	−	1	+	1	1	0	1
d	0	+	1	+	0	0	0	0

Schenck[15,16] has reported light-induced *in vitro* synthesis of a considerable number of different organic peroxides in the presence of oxygen and some sensitizing substance. Since organic peroxides are known to produce chromosomal aberrations in bean roots[13,17], it seems possible that such compounds are involved in the photodynamic induction of structural chromosome changes.

A radiomimetic effect of acridine orange has been reported by D'Amato[18], working with onion root-tips as experimental material. Since D'Amato performed his experiments "in the ordinary conditions of diurnal illumination", it seems possible that in his experiments, too, the radiomimetic effect of acridine orange was due to its ability to act as a photosensitizing substance. In the present study, acridine orange was inactive in the absence of light.

Because of the respiratory activity of the cells, the oxygen concentration is likely to be considerably lower in the central parts of an organized tissue such as a bean root than in the solution surrounding the tissue. The existence of such an oxygen gradient in respiring tissues explains why the X-ray sensitivity of bean roots is influenced by much lower concentrations of oxygen in the presence, than in the absence, of a respiratory inhibitor[10,19].

In order to find out if structural changes in chromosomes can be induced photodynamically at lower oxygen concentrations when respiration is inhibited, a number of experiments were performed with cupferron (the ammonium salt of N-nitroso phenylhydroxylamine) as a respiratory inhibitor. The results appear in Table 2. In the 45-min. experiments, the cupferron treatments were of the same duration as the period of illumination. When the roots were illuminated for 30 min. only, the duration of the cupferron treatments was 40 min. Previous experiments have shown that cupferron is a radiomimetic agent in the presence of oxygen[13,20]. However, in order to obtain a marked radiomimetic effect, it is necessary to have higher concentrations of cupferron and higher treatment temperatures as well as longer periods of treatment than those used in the present study (400 μM; 15–18° C.; 40–45 min.).

Table 2 shows that in the absence of either light or oxygen there is no marked effect of cupferron on roots which have not been pre-treated with acridine orange (IV*b*, V*c*). There is some evidence that the radiomimetic effect of cupferron in the presence of oxygen is somewhat increased by light (V*a* and unpublished results). In the absence of light, no marked effect is obtained with cupferron on roots pre-treated with acridine orange (II*b*, IV*c*, V*d*). However, when roots pre-treated with acridine orange were illuminated in the presence of cupferron but in the absence of oxygen (oxygen-free nitrogen bubbled through the solution), the magnitude of the effect obtained was of the same order as that produced by 100 r. of X-rays in air, which is close to the upper limit of what can be conveniently scored (I*a*, II*a*, III*a*, IV*d*). When oxygen was introduced into the system the effect decreased. At 1 per cent oxygen in the gas phase, the effect was still about the same as that obtained in the absence of oxygen (I*b*, IV*e*), but when the oxygen concentration was 20 per cent or more, the effect was no stronger than that obtained in the absence of cupferron (Table 1, Table 2 : I*c*, I*d*).

The fact that the highest frequency of aberrations was obtained when oxygen-free nitrogen is bubbled through the solution suggests that in the presence of cupferron there is some other mechanism than that involving oxygen by which light energy absorbed by acridine orange can be used for the production of chromosomal aberrations. This would mean that, in contrast to the results summarized in Table 1, those obtained in the cupferron experiments are not explainable by the peroxide hypothesis.

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ANIMAL PHYSIOLOGY

Hyperglobulinæmic Thrombo-Hæmorrhagic Diathesis

In reviewing the literature of the hyperglobulinæmias one is struck by the frequency of the reports of a concomitant hæmorrhagic diathesis. In a survey by us of more than a thousand cases of macroglobulinæmia, cryoglobulinæmia, visceral leishmaniasis and miscellaneous hyperglobulinæmias, a hæmorrhagic diathesis was reported in 63–94 per cent of the cases in each category. These observations suggest that purpura is a general phenomenon in the presence of increased plasma globulins.

Thromboses, in addition to hæmorrhages, were reported in 3–21 per cent of the cases. This coincidence of thromboses and hæmorrhages is of sufficient moment to warrant its consideration as a clinical entity for which the name hyperglobulinæmic thrombo-hæmorrhatic diathesis is suggested. We have also observed both thromboses and hæmorrhages in a group of patients reported elsewhere[1,2].

An explanation of this observation is suggested by the experimental studies made in this laboratory which have shown that some globulins have the ability to combine with clotting factors. The hypothesis is proposed that in a variety of clinical conditions γ-globulins are produced which acquire the ability to combine with clotting factors. When such associations occur, the clotting factors are withdrawn from active participation in clotting and hæmorrhages ensue. When such combinations dissociate, large amounts of clotting factors are released suddenly into the blood-stream and the situation becomes thrombotic. When both association and dissociation are occurring, the clinical picture would include both hæmorrhages and thromboses, that is, a thrombo-hæmorrhagic diathesis.

8 patients with euglobulin have been studied; 2 with macroglobulinæmia, 2 with multiple myeloma, 1 with alcoholic liver cirrhosis, 1 with rheumatoid arthritis and 2 with myocardial infarctions. One of the myeloma cases had a cryo-fibrinogen-globulin complex as well as the euglobulin.

The following behaviour characteristics of the unusual euglobulins studied are significant.

(1) These proteins have the ability to complex with, and co-precipitate, clotting factors. Precipitation of the euglobulin from the patient's plasma, or from normal plasma to which it was added, reduced the concentration of clotting factors remaining in the plasma. These clotting factors were demonstrable in the solution of the precipitated euglobulin.

(2) The euglobulins can combine with and remove from the plasma active accelerin, its precursor proaccelerin, prothrombin and convertin. The amounts and proportions of the clotting factors involved vary from case to case.

(3) Some results suggest that this association of euglobulin with clotting factors occurs *in vivo* as well as on precipitation of the euglobulin. It was frequently observed that the sums of the accelerin and proaccelerin concentrations in the solution of the euglobulin and in the plasma freed of euglobulin were greater than the concentrations in the whole plasma. This phenomenon was also seen when precipitation of the euglobulin did not reduce the plasma accelerin- or proaccelerin-level, but when appreciable amounts of these factors were found in the euglobulin. In one case, a high level of prothrombin activity was demonstrable in the euglobulin precipitated from serum when the residual serum prothrombin was nil. In another case, more accelerin, proaccelerin and convertin were measurable in serum euglobulin and euglobulin-free serum than in the whole serum. The clotting factors present in excess of the measurable plasma- or serum-levels represent the amount which was held *in vivo* by the euglobulin.

(4) The possibility of *in vivo* inhibition of clotting factors by euglobulin has been suggested by instances of increased prothrombin, convertin and proaccelerin after the removal of euglobulin.

The clotting abnormalities are usually, but not always, associated with increased total plasma proteins. 2 of the 8 patients studied had normal total protein-levels; all but one had increased γ-globulins. Comparison of the quantities of euglobulin present with the amount of clotting factor activity coprecipitated indicates that euglobulin of the order of 100 mgm. per cent can contain as much as 600 per cent of proaccelerin.

A globulin which complexed with fibrinogen to form a cold precipitable complex was first reported in one of these cases of multiple myeloma[1]. This observation has been confirmed by Firkin[3] in a case of essential cryoglobulinæmia. On the basis of the concept presented here, dicumarol was used by Domz and Feigin[4] in a case of essential cryoglobulinæmia with Raynaud's phenomenon, cyanosis and necrosis of the fingers. There was an immediate response to the therapy with complete relief of the pain within 48 hr., followed by rapid healing of the fingers.

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Recurrent Inhibition in Cerebral Cortex

RECURRENT inhibition via interneurones (Renshaw cells) was recently invoked by Brooks and Wilson[1] to account for changes in monosynaptic spinal reflexes following antidromic activation. This mechanism, which confines stretch reflexes to their paths of afferent origin, operates through a cholinergic synapse between the motoneurone axon collateral and the Renshaw cell[2], which liberates an unknown inhibitory transmitter. Presumably the same mechanism functions with respect to disynaptic pathways through the cord. The purpose of this communication is to describe an analogous system in the cerebral cortex of dogs, operated under ether and immobilized by succinylcholine.

During experiments on the interaction between antidromic volleys in the medullary pyramids[3] recorded with cortical microelectrodes, and impulses from the thalamic nucleus ventralis lateralis[4], antidromic inhibition of cortical re-excitation[5] and directly excited cortical activity were noted[6]. In the present experiments the pathway from the thalamus to the corticospinal tract via the cortical projection of the nucleus ventralis anterior was used as a test. This has been presumed to be disynaptic with one interposed neurone. The antidromic volley was delivered via one bundle of corticospinal fibres, separated from the pyramid. The ventralis anterior was stimulated bipolarly, and the responses recorded in the remainder of the medullary pyramid (Fig. 1, *A* and *B*). It was found that the anticholinergic drug, dihydro-beta-erythroidine hydrobromide, reduced the magnitude of antidromically elicited inhibition in this 3-neurone arc. The drug was given in the ipsilateral carotid artery in amounts of 0·5 mgm./kgm. following isolation of the internal carotid circulation. Antidromic inhibition, as judged both by the decreased rate of discharge in the corticospinal tract to pyramidal stimuli of increasing frequency and by the amount of hyperpolarization of cortical neurones recorded with intracellular electrodes[3], was increased by 20–30 μgm. of acetylcholine chloride, and increased still further by 0·2–0·5 mgm./kgm. of eserine sulphate, given intra-arterially (Fig. 1, *C*). With increasing frequency of stimulation of the medullary pyramid the probability of firing of single gigantopyramidal neurones dropped, according to a parabolic function, over the frequency-range of 30–40 c./s. The same effect was obtained from bipolar stimulation of the cortex at a depth of 1·0–1·3 mm.

Further, the inflexion in the rising phase of intracellular pyramidal neurone spikes was increased by antidromic and deep cortical stimulation. This represents hyperpolarization.

Since the Renshaw mechanism in the cortex cannot be substantiated without physiological demonstration of the inhibitory interneurones, the cortical layers were systematically mapped during the above-mentioned pyramidal hyperpolarization of cells. Rapidly discharging units were found at depths corresponding to cortical layers III and IV in the dog 'motor' and 'premotor' areas (Fig. 1, *D*). These units were active during hyperpolarization of primary neurones. Further pharmacological studies showed that the hypothetical inhibitory synapse was blocked by picrotoxin, strychnine and tetanus toxin, the latter two drugs having been used in the spinal cord by Eccles with similar results[2]. A detailed description of this and related findings is in preparation.

Histological evidence for a cortical Renshaw system was also sought. Cajal demonstrated the endings of pyramidal neurone collaterals on short-axon neurones, and functional evidence for their existence is abundant[5]. The existence of star-cell axons (assumed to be interneurones) upon the apical dendrite of pyramidal cells in the same or next lower layer has also been shown (Fig. 2, *A*). Recent work[7] has indicated that much, if not all, of the activity at axo-dendritic synapses relates to the creation of long-standing hyper- or de-polarization of the apical dendrites. It has also been suggested[8] that such changes are due to the activity of excitatory or inhibitory interneurones, although no physiological or anatomical arrangement of these has been put forth which would account accurately for most of the results concerning cortical activity.

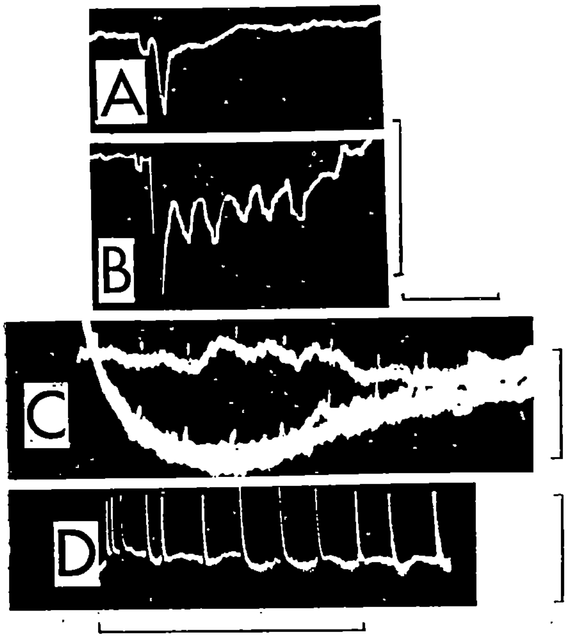

Fig. 1. *A*, Response recorded in one bundle of medullary pyramid fibres following stimulation of remainder of pyramid and stimulation of the ventralis anterior. *B*, Same response after 0·5 mgm./kgm. dihydro-beta-erythroidine hydrobromide. Note increased amplitude of surface positive and oscillating (interneuronal) responses. For *A* and *B* time mark is 8 msec. *C*, Potentials generated in a gigantopyramidal neurone (responding to pyramidal stimulation) by an antidromic volley (40 c./s.) in corticospinal fibres recorded between an intracellular electrode and an indifferent point. Horizontal superposed traces were obtained before antidromic stimulation. Intracellular negativity downward in this and following record. The latency of this hyperpolarization is 0·9–2·0 msec. following activity of cells in deeper layers. Msec. time marks. Potential calibration, 5 mV. *D*, Discharges of a cortical inhibitory interneurone, recorded intracellularly at a depth of 1·1 mm. in dog motor cortex, following antidromic volley in corticospinal tract. Time mark, 20 msec., potential calibration, 30 mV.

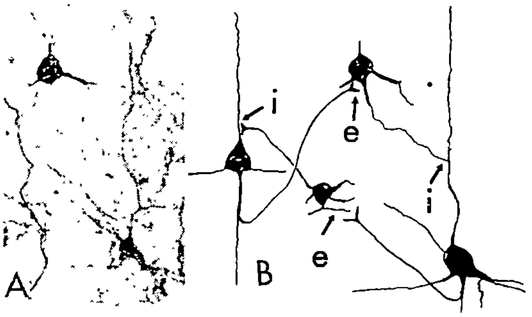

Fig. 2. *A*, Photomicrograph of cat visual cortex (by courtesy of Dr. E. Ramon-Moliner, Montreal Neurological Institute), modified Golgi Cox stain, showing ending of star-cell axon in layer IV upon apical dendrite of pyramidal neurone in layer V. Arrows trace course of axon. (× 125). *B*, postulated anatomical arrangement for a cortical recurrent inhibitory system. Inhibitory endings, *i*; excitatory (cholinergic) endings, *e*

It is not postulated that this inhibitory mechanism, which had been suggested by Phillips[3] and others, is the only, or even the most widely active, means for cortical inhibition. However, these results, in addition to a large number of supporting observations which are less rigorous, make its existence most likely. Its proposed structure and operation are outlined semidiagrammatically in Fig. 2, *B*. Inhibitory endings are thought to exist primarily on neighbouring or remote neurones, rather than on the neurone the collateral of which activates the inhibitory cell. Cells firing to afferent impulses would excite neighbouring cells until the inhibitory mechanism reduced the activity multiplication factor to one. Firing cells inhibit neighbours, and are thereby protected from inhibition. In this manner a small group of cells with inhibitory interconnexions could maintain a relatively constant firing-rate without necessitating reverberation or re-entry circuits, which might nevertheless exist. It is suggested further that the hyperpolarization exerted by inhibitory interneurones has only a partial effect upon, but does not alone control, the basal firing rhythm[6] of primary cortical neurones. Electrocorticographical findings which support this concept have been obtained[9] and a similar arrangement based on theoretical considerations has been independently described by Milner[10].

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Synthesis of Dextran Sulphate labelled with Carbon-14 and Tracer Experiments in the Rat

PREVIOUS experiments[1,2] with the heparinoid anticoagulant, dextran sulphate, in experimental animals and man have established that between 40 and 50 per cent of a single intravenous dose of dextran sulphate of a molecular size suitable for clinical use was excreted in the urine in 48 hr.

Autoradiographs of the tissues of animals given dextran sulphate of similar molecular characteristics labelled with sulphur-35 suggested that the portion of the dose unaccounted for by urinary excretion was broken down within the body but that the ^{35}S-sulphate residue was retained in the general body pool of ester sulphate since, as with the administration of $Na_2{}^{35}SO_4$ [3], radioactivity was demonstrable in gastric mucin, skin and, to a lesser extent, in cartilage (Walton, unpublished work). This redistribution of the labelled sulphate residue rendered difficult the interpretation of the results obtained in terms of the distribution of dextran sulphate in the tissues. Accordingly, further experiments have been undertaken using dextran sulphate labelled in the dextran part with carbon-14.

^{14}C-Dextran was prepared by inoculating an aqueous buffered medium containing yeast extract and ^{14}C-sucrose (3·76 gm., 3·3 mc.) with *Leuconostoc mesenteroides* and incubating the mixture for 3 days at 25° C. ^{14}C-Dextran and protein were precipitated with ethanol. The precipitate was redissolved and freed from protein by treatment with trichloracetic acid yielding 1·162 gm. ^{14}C-dextran with a specific radioactivity of 22·39 mc./mole of carbon.

The ^{14}C-dextran so obtained was partially hydrolysed with *N*/1 sulphuric acid and fractionated by the addition of successive increments of acetone. A fraction (232 mgm.) of viscosity comparable to that used for the preparation of clinical dextran sulphate was selected for sulphation by treatment with chlorosulphonic acid in pyridine as previously described[4].

The ^{14}C-dextran sulphate (413 mgm.) (found: C, 20·40; H, 2·15; S, 16·85. $[C_6H_{8\cdot16}O_5\,(SO_3Na)_{1\cdot84}]_n$ requires C, 20·59; H, 2·35; S, 16·86 per cent) had a specific radioactivity of 22·39 mc./mole carbon or 0·45 µc./mgm. and an anticoagulant activity of 13 units/mgm. Paper chromatography revealed results similar to those obtained with the dextran sulphate previously employed[2].

A male albino rat weighing 273 gm. was injected intravenously via the tail-vein with a solution of ^{14}C-dextran sulphate (5 mgm., that is, 2·25 µc. and dose equivalent to 18·3 mgm./kgm./body-weight) in saline and placed immediately in a closed-circuit apparatus[5], allowing collection of the respired air. The rat was maintained thus for 48 hr., being allowed access to food and water *ad libitum*. The expired carbon dioxide was collected in 3 *N* sodium hydroxide and converted into barium carbonate. Aliquots were used for the determination of specific radioactivity.

At the end of the experimental period the animal was killed by a blow on the head, various organs were removed, weighed and portions homogenized by grinding under liquid air. Other portions were submitted to histological examination which confirmed that the injected material, like previously tested examples of dextran sulphate for clinical use[6], was not segregated in reticulo-endothelial cells.

Table 1. LABELLED CARBON CONTENTS OF RESPIRED CARBON DIOXIDE AND OF TISSUES OF RAT FOLLOWING INJECTION OF 5 MGM. (2·25 µC.) OF ^{14}C-DEXTRAN SULPHATE IN EXPERIMENT LASTING 48 HR.

Source	Weight (gm.)	Carbon content (per cent)	Specific radio-activity (µc./mole carbon)	Total radio-activity (µc.)	Concentration of injected radio-activity (per cent)
Carbon dioxide respired	125·674	6·085	0·13	0·08	3·55
Liver	13·366	13·35	1·19	0·18	8·0
Spleen	0·650	9·15	1·00	0·005	0·22
Lungs	2·810	9·08	0·19	0·004	0·18
Kidneys	2·423	23·20	1·68	0·08	3·55
Muscle (sample)	1·120	9·73	0·17	—	—
Total musculature	123·94*	—	—	0·17	7·56
Bone (femur)	0·86	5·62	0·15	—	—
Whole skeleton	14·80*	—	—	0·01	0·44

Total radioactivity accounted for: 23·50 per cent of dose.
* Average figure derived from published data, ref. 10.

^{14}C-Dextran and ^{14}C-dextran sulphate were burned in a stream of oxygen free of carbon dioxide, and aliquot parts of the homogenized tissues were treated with boiling chromic acid combustion fluid[7]. The carbon dioxide produced in each case was converted into barium carbonate and the radioactivity determined by the infinitely thick disk method[7-9] using an end-window counter and a sample of poly-(^{14}C-methyl) methacrylate supplied by the Radiochemical Centre, Amersham, as a standard source for barium ^{14}C-carbonate. The results tabulated are corrected for background and paralysis time of the counting equipment.

Excretion of carbon dioxide labelled with carbon-14 in the expired air indicated complete oxidation of a portion of the administered ^{14}C-dextran sulphate. The rate at which this occurred appeared to be somewhat slower than the rate of excretion of labelled carbon dioxide from ^{14}C-dextran in rats since 3·55 per cent of the injected dose of ^{14}C-dextran sulphate was accounted for after 48 hr. in the present experiment as compared with 8–10 per cent of ^{14}C-dextran[11] in the same period. The radioactivity of the expired air together with that found in the organs examined accounted for 23·50 per cent of the dose administered. Assuming urinary excretion of a further 40–50 per cent in the first 48 hr. as previously found[1,2] about 30 per cent remained unaccounted for and presumably was distributed in the body fluids and tissues not sampled.

The distribution of radioactivity in the tissues suggested that the major sites of retention (and therefore possibly of metabolism) of the material were in the liver and in muscle (8 per cent each), as has also been found for ^{14}C-dextran[11]. High retention in the liver has previously been found for other labelled polysaccharide sulphates (namely, 7·2 per cent for cellulose ^{35}S-sulphate[12] and 9·0 per cent for one preparation of low molecular weight xylan ^{35}S-sulphate[13]). The significance of the relatively high radioactivity found in the kidneys in the present experiment (3·55 per cent) is less clear since this might be accounted for partly by this organ being the one chiefly concerned in the excretion of dextran sulphate[2] and therefore probably containing ^{14}C-dextran sulphate in process of excretion in the urine.

The sample of dextran sulphate used for the experiments described underwent decomposition before further biological experiments could be carried out. It seems likely that decomposition was initiated by self-irradiation and continued autocatalytically under acidic conditions. Details of this work will be published elsewhere.

We thank Profs. M. Stacey and J. R. Squire for their interest and for providing facilities. We are indebted to Prof. E. J. Bourne and Dr. C. R. Ricketts for helpful discussions throughout the work, and to Dr. W. F. R. Pover for advice and the loan of the closed-circuit apparatus used. We also acknowledge gratefully generous financial assistance from Messrs. Glaxo Laboratories, Ltd., for this work.

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Passive Antibody Decay in Thyroidectomized Rabbits

In the course of an investigation of the immune response of rabbits exposed to a low environmental temperature (– 15° C.) it was noted that the decay-rate of passively administered homologous antibody was increased[1]. Reference has been made to the fact that thyroxin-treated rabbits also exhibit an increase in passive antibody decay[2]. The fact that an animal metabolizes protein more rapidly under conditions of cold stress or when treated with thyroxine leads one, *a priori*, to consider more closely the influence of the thyroid on the immune response under cold stress. The following preliminary investigation was therefore undertaken to determine the effect of surgical thyroidectomy on the rate of decay of passively administered homologous antibody.

Adult male rabbits weighing 2·5–3·0 kgm. were used in this study. Five were surgically thyroidectomized and allowed to recuperate for 2–3 weeks before being injected with antibody, at which time their metabolic rate was approximately 75 per cent of normal. Ten untreated rabbits were used as controls.

The antibody used in this study was homologous γ-globulin prepared from high-titre anti-bovine serum albumin rabbit serum by one-third saturation with ammonium sulphate at *p*H 7·8. The γ-globulin so obtained was reprecipitated twice, dissolved in 1 per cent pyrogen-free sodium chloride, and the residual ammonium sulphate removed by dialysis against 1 per cent sodium chloride. Each animal was injected intravenously with 15 ml. of the γ-globulin solution, which contained approximately 170 mgm. of precipitable antibody protein. The animals were bled at intervals and the circulating antibody concentration estimated by the quantitative micro-precipitin analyses by a modification of the method of Lanni *et al.*[3]. The results were plotted semi-logarithmically as the percentage of the injected dose remaining in the circulation versus time (Fig. 1). The slope of the linear portion of the curve (assumed to represent steady-state loss of antibody) was calculated by the method of least squares, extrapolated back to zero time, and half-life values calculated from that point.

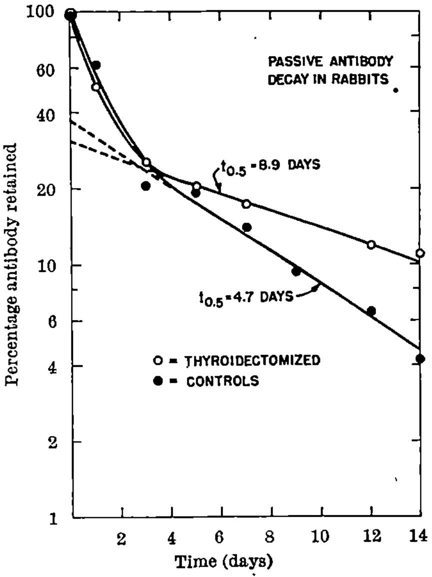

Fig. 1. Semi-logarithmic plot of percentage of injected antibody remaining in circulation versus time in days

The half-life of passively administered homologous antibody in the thyroidectomized rabbits was 8·9 ± 0·4 days compared to 4·7 ± 0·2 days for the untreated controls.

Previous work by others has indicated that thyroxin decreases and propylthiouracil increases antitoxin production in rabbits, but has the opposite effect in guinea pigs[4]. This species difference is attributed in part to a thyroxine-induced adrenocortical hyperactivity, which may have a greater effect in depressing antibody production in the 'cortisone-sensitive' rabbit than in the 'cortisone-resistant' guinea pig. The significance of these results and our own in relation to the immune response under stress conditions raises the question as to whether a change in circulating antibody-level would be due primarily to an alteration in the antibody-forming mechanisms, or would be due to the effect of these conditions on the mechanisms responsible for antibody decay. If the changes in antibody decay are considered as being superimposed on an essentially normal rate of antibody production, the net result would be an apparent decrease in the immune response of thyroxin-treated rabbits and an apparent increase in the immune response of hypothyroid rabbits. If, on the other hand, there is also an alteration in the rate of antibody production, then the net result would be either an accentuation of the immune response, if antibody production was affected in the opposite direction, or perhaps no observable difference, if a change in antibody decay was offset by a change in antibody production in the same direction, that is, an increase in antibody decay compensated by an increase in antibody production. Further study on the influence of the thyroid on the immune response is indicated, and experiments on active antibody production are now in progress.

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Balance Trials with Magnesium-28 in Sheep

Fæcal magnesium comprises two fractions, an endogenous fraction originating from the body and excreted into the gut and an exogenous fraction representing unabsorbed dietary magnesium. Once the relative proportions of these two fractions are known, it is possible to calculate both the endogenous fæcal magnesium and the true availability of dietary magnesium. A method for determining these proportions would seem to be the comparative balance technique[1], since this could be adapted for magnesium-28 provided the quantity of this isotope in a single dose was sufficient for accurate determination of the total eliminated in the fæces after either oral or intravenous administration. As the cost of magnesium-28 is very high the size of dose for economic reasons must be small, but this communication describes experiments which would appear to be satisfactory from both points of view.

Cyclotron-produced 'carrier-free' magnesium-28 was used, and initially the doses contained 80 μc., but after chemical separation and transit, only about 30–40 μc. remained for administration into the sheep. The cost of each dose was £30.

Trials were carried out with one sheep, an adult North Country Cheviot wether, which received a constant diet of hay supplying 0·77 gm. of magnesium a day throughout the experiment. Single doses of magnesium-28 were given at 8.40 a.m., either into the rumen through a fistula, or into the jugular vein by means of a nylon catheter. The fæces and urine were collected twice daily at 8.40 a.m. and 4.40 p.m. and their radioactivity determined in a modified ring counter[2].

After ruminal administration it was found that magnesium-28 could be followed in the fæces for 5 days only. Nevertheless, it was possible to calculate the magnesium-28 still to be eliminated in the fæces since the ratio of magnesium-28 to dry matter in the fæces declined exponentially after reaching a peak on the second day after administration. This can be expressed by the following equation:

$$R = 0{\cdot}304 \exp(-0{\cdot}0306t)$$

where R is magnesium-28 recovered in fæces/magnesium-28 administered × 100/fæcal dry matter and t is time after administration (hr.).

Of the original dose, 62·6 per cent was recovered from the fæces within the period 2–5 days after administration, and it was calculated by integration of the above formula that a further 3·4 per cent would be eliminated by the same route after 5 days. These, together with the 13·2 per cent passed out on the first day, make a total of 79·2 per cent of the ruminal dose eliminated in the fæces. In the first 5 days, 0·07 per cent was excreted in the urine. Over the same period the fæcal non-radioactive magnesium represented 100·8 per cent of the dietary intake.

Following intravenous injection, urinary magnesium-28 could be followed for 5 days and fæcal magnesium-28 for 4 days 8 hr., and over this period 11·9 and 19·4 per cent of the given dose were excreted by the separate routes. The value for urinary magnesium-28 is much greater than those reported for calcium-45 in cattle[3], suggesting that the urinary route of excretion is more important for magnesium than it is for calcium.

The calculated values for the endogenous fæcal magnesium and the availability to the sheep of the magnesium present in hay were 205 mgm./day and 25·8 per cent respectively. These values are in good agreement with those determined for similar sheep by Field *et al.*[4] using indirect methods.

The evidence presented here shows that the true availability of dietary magnesium can be determined with magnesium-28, but its use will be limited by its high cost and its short half-life, which results in a severe reduction of its radioactivity in transit.

My thanks are due to Dr. J. R. Greening and Mr. P. Tothill, Department of Medical Physics, University of Edinburgh, for their valuable help.

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Metabolism of Benzene Hexachloride by Resistant Houseflies *Musca domestica*

Our previous work on the metabolism of isomers of benzene hexachloride by a resistant strain of houseflies showed that the α- and γ-isomers are rapidly converted to water-soluble metabolites[1–3], and in the course of the reaction chloride ions are formed in the proportion of four or more per molecule of benzene hexachloride metabolized[4]. We have now found that alkaline hydrolysis of the metabolic products produces dichlorothiophenols.

The method of isotopic dilution was used for identifying the thiophenols, which have not yet been isolated. The Jealotts Hill strain of flies resistant to benzene hexachloride[5] was exposed to α- or γ-benzene hexachloride labelled with carbon-14 in a closed flask for 24 hr. and then extracted with 80 per cent ethanol. To this extract was added 200 mgm. of pure unlabelled dichlorothiophenol and the mixture subjected to alkaline hydrolysis with sodium hydroxide at 100° C. for 30 min. The dichlorothiophenol was then converted to a derivative, either by oxidation with iodine to the disulphide $(Cl_2C_6H_3S)_2$ or by reaction with chloroacetic acid to the dichlorophenyl thioglycollic acid $(Cl_2C_6H_3.S.CH_2.CO_2H)$. The derivative was isolated and repeatedly crystallized until the radioactivity measured in a flow-type proportional counter could no longer be reduced, even with change of crystallizing solvent.

Each of the six dichlorothiophenols was tested in this way with the results shown in Table 1.

Table 1. DICHLOROTHIOPHENOLS PRODUCED BY ALKALINE HYDROLYSIS OF METABOLITES OF BENZENE HEXACHLORIDE FROM HOUSEFLIES RESISTANT TO γ-BENZENE HEXACHLORIDE

Position of chlorine atoms	Percentage of total water-soluble benzene hexachloride metabolites	
	α-Benzene hexachloride	γ-Benzene hexachloride
2 : 3-	2*	< 1*
2 : 4-	20* 21†	32*
2 : 5-	21* 19†	16* 14†
2 : 6-	5*	9*
3 : 4-	19* 22*	5* 4†
3 : 5-	< 2*	< 2*

* Using thioglycollic acid derivative.
† Using disulphide derivative.

The figures show that alkaline hydrolysis of metabolites of benzene hexachloride produce dichlorothiophenol amounting to approximately 68 per cent of the water-soluble products from the α-isomer and 61 per cent from the γ-isomer. It is inferred that the metabolism of benzene hexachloride by the flies to produce water-soluble compounds involves the formation of a C—S bond. The nature of the initial metabolic product is not known; but it is suggestive that aryl mercapturic acids produced from halogen compounds in mammalian detoxication processes[6] are converted to thiophenols by alkaline hydrolysis[7].

A scheme which would satisfactorily account for the production of dichlorothiophenols from benzene hexachloride is set out below, but it is emphasized that we have at present no evidence in support of this other than that offered above.

$$C_6H_6Cl_6 + HS\mathit{R} \rightarrow C_6H_6Cl_5.S.\mathit{R} \rightarrow C_6H_3Cl_2SH + \mathit{R}OH + 3HCl$$

In this reaction the nature of *R*SH is unknown, but it is possible that the compound may be reduced glutathione. This compound, which has been shown by Kearns and his colleagues[8] to be essential for the *in vitro* enzymatic conversion of DDT to its monodehydrohalogenation product DDE, we now know to be essential also for the benzene hexachloride process *in vitro*.

Following in detail the methods employed by Kearns we have been able to convert α- and γ-benzene hexachloride to water-soluble compounds *in vitro* using fly macerates, acetone powders prepared from macerated flies, and impure enzyme preparations made from fly extracts by cold fractional precipitation with ammonium sulphate. The products of the *in vitro* enzyme reactions have been shown to yield thiophenols by alkaline hydrolysis. The *in vitro* reaction did not proceed in the absence of added glutathione.

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Effect of Chloral Hydrate on Growth of Hair

STUDIES on the percutaneous toxicity of liquids applied as small (100μ) droplets to the guinea pig have shown that the presence of hair prevents some of the droplets from reaching the skin. Consequently, when the test liquid is applied in this droplet size, it shows less toxicity than an equivalent weight of large (400μ) droplets[1].

In percutaneous toxicity studies in the guinea pig, it is usual in this laboratory to apply the test liquid to animals 24 hr. after they have been clipped or chemically depilated. This 24-hr. period is allowed to minimize the effects on the skin of the hair-removal procedures. Although some species, such as the rabbit, show no appreciable hair growth 24 hr. after depilation, a very considerable growth occurs in the guinea pig.

The present experiment was conducted to determine whether or not this rapid regeneration of hair could be prevented. The inhibiting drug chosen for the investigation was chloral hydrate. Butcher[2], in studies on the hair cycle of the rat, reported that the hair follicles were inactivated by the subcutaneous injection of this drug. He did not mention the dosage used, or the duration of the treatment. The dosages chosen for the present experiment were 50 mgm./kgm. and 100 mgm./kgm., which are well below the hypnotic dose[3] of 250 mgm./kgm.

As test animals, 12 male and 12 female guinea pigs weighing 700–800 gm. were chosen. They were divided into three groups each with 4 males and 4 females. The animals in one group received 100 mgm./kgm. of chloral hydrate, those in another group 50 mgm./kgm. of the drug and the third was the control group. The chloral hydrate was dissolved in saline (160 mgm./c.c.) and daily injections were made subcutaneously for 14 consecutive days. On the fifteenth day, all animals were depilated with a barium sulphide paste. 24 hr. later, it was noted that the control animals all showed the usual rapid hair growth, whereas in all the animals treated with the drug the growth was inhibited to a considerable extent. No differences in effect could be noticed between the two dosage-levels, nor between male and female animals.

Several depilated animals were observed over a period of 6 days in order to study the effect of the drug on subsequent regrowth of hair. It is quite evident that the inhibiting action of the drug persists for at least 7 days after its administration has been discontinued.

The results of the present experiment indicate that, by using guinea pigs treated with chloral hydrate, the comparative percutaneous toxicity of large and small droplets of liquid chemical substances may be investigated without the interfering effect of hair.

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Crystals of Riboflavin making up the Tapetum Lucidum in the Eye of a Lemur

The tapetum lucidum of the eye is a specialized layer lying behind, but adjacent to, the light-sensitive cells of the retina. It is specialized to form a reflecting surface so that any light not absorbed during its first passage through the light-sensitive cells is reflected back again and has a second opportunity to be absorbed. The tapetum is the basis of eye-shine in animals ; it may be made up of crystals or of regularly arranged fibres[1,2]. Many fish, for example, have tapeta made of crystals of guanine, carnivores one of crystals of a complex of zinc-cysteine[3], while herbivores such as the sheep and cow have fibrous tapeta. Man and the higher apes have no tapetum ; but some lemurs have a well-developed one ; the brilliant yellow tapetum of *Galago monteiri* is described by Johnson[4], who says " . . . the background resembles burnished gold". Rochon-Duvigneaud[5] has found that both diurnal and nocturnal lemurs may have a tapetum. Kolmer[6] agrees with this and notes that the tapetum of *Lemur rufifrons*, a diurnal lemur, is both crystalline and yellow. Luck[7] has found that the eyes of *Galago crassicaudatus agisymbanus*, a nocturnal lemur, have a fluid vitreous body and a highly developed cellular tapetum which is brilliant gold in colour.

Through the kindness of Prof. C. P. Luck, I have examined the eyes of this lemur *Galago crassicaudatus agisymbanus*, and the evidence suggests that the tapetum is made of crystalline riboflavin.

Examination in vivo. The fundus of the eye viewed ophthalmoscopically shows a brilliant yellow-green central area with a peripheral pigmented part. With pupils dilated and in sunlight a green-yellow reflexion can be seen ; this is also observable, though less marked, if ultra-violet light from a mercury arc lamp is shone into the eye, which makes it probable that the light reflected through the pupil is due at least in part to fluorescence.

Examination in vitro. The central area of the fundus in the opened eye is brilliant yellow. When the retina is removed the brilliance is more marked and is, as Johnson says, like burnished gold. Much of the yellow material can be brushed or scraped off the underlying choroid and when examined microscopically with polarized light shows flat crystalline plates of irregular size (Fig. 1). Where the plates overlap they are yellow. Using acetone as fixative, sections can be made showing crystals lying immediately behind the retinal pigment epithelium, which is devoid of pigment in the central tapetal area. The crystals were, however, irregularly arranged, totally lacking in some parts and appearing more like needles or rods than flat plates (Fig. 2) ; probably even acetone fixation allows some solution and rearrangement of the crystals. When examined under ultraviolet light the crystals in the section of the eye fluoresced bright yellow.

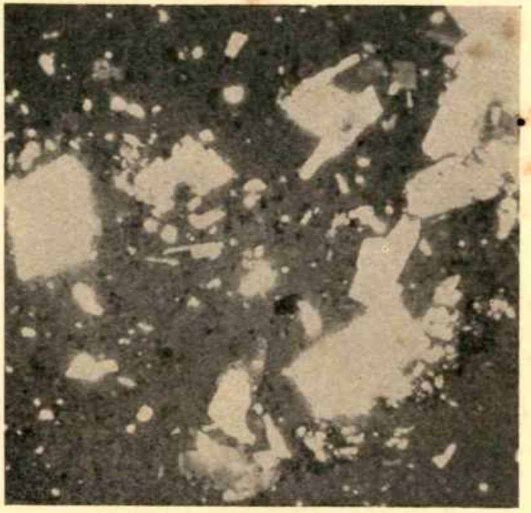

Fig. 1. Crystalline material brushed off the tapetum of *Galago crassicaudatus* and examined with polarized light

Identification of crystals as riboflavin. The yellow material either from tapetal material dried in acetone or from the tapetal scrapings was dissolved in water or 1 per cent formic acid. Such solutions are yellow and show yellow-green fluorescence. The absorption curve in 0·1 per cent formic acid showed peaks at 266 mμ, 370 mμ and 445 mμ, the peak at 266 mμ being the greatest. Light of 285 mμ, 395 mμ and 470 mμ was used to elicit fluorescence at 530–550 mμ. Both the absorption curve and the fluorescence corresponded with those of riboflavin determined at the same time. Duggan *et al.*[8] give 520 mμ as the fluorescence maximum of riboflavin ; it is probable that the

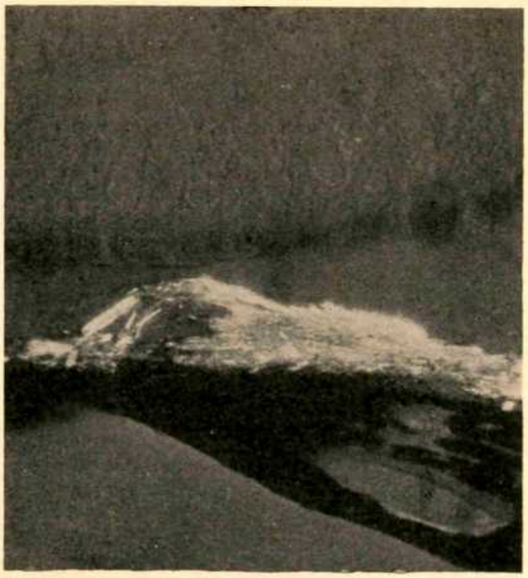

Fig. 2. Section of eye of *Galago crassicaudatus* showing crystalline tapetum lying between the retina and the choroid (polarized light)

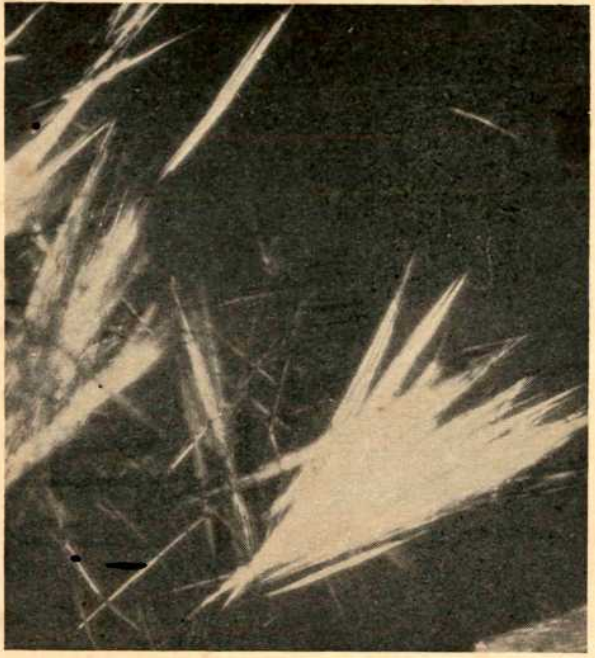

Fig. 3. Crystals deposited from solution of tapetal material in 1 per cent formic acid

maximum at 530–550 mμ found in experiments is due to slight instrumental error. The tapetal material corresponded exactly with free riboflavin in solubility, chromatographic behaviour, formation of a chloroform-soluble substance on irradiation with ultra-violet light in alkali and of a blue fluorescent substance on irradiation in acid, and in being reversibly reduced to a colourless, non-fluorescent substance by sodium hydrosulphite.

It seemed, therefore, probable that the crystalline tapetum lucidum of this lemur is made of riboflavin. The only divergence is of crystal form. Typical riboflavin crystals are needles and such needles were deposited from a 1 per cent formic acid solution of the tapetal material (Fig. 3); but the fresh tapetum itself, scraped off and examined at once, contained only plates. As the tapetum of carnivores and the choroids of some fish[9] contain very large amounts of zinc, the formic acid extract of the tapetum was examined spectrographically to see if any metal was present in abnormally large amount, but none was found. However, it seemed possible that the plate crystals of the tapetum contained riboflavin in association with some other substance. Mrs. D. M. Hodgkin very kindly took X-ray powder photographs of the tapetal material, fresh from the eye, and finds it to be identical with one of the plate forms of riboflavin obtained by recrystallizing a commercial preparation. Sakate[10] has noted plate forms of riboflavin.

Crystals of riboflavin have been described in cells of the fungus of *Erymothecium ashbyii*[11], and Euler and Adler[12] noted that the eyes of many fish contain a high concentration of riboflavin but did not report crystals. Apart from the fungus, the tapetum of this lemur seems to be the only biological material where crystalline riboflavin has been found. Riboflavin is soluble in water to 19 mgm./100 ml. at 40° C. and the biochemical reactions which deposit and maintain it as crystals in the tapetum are unknown.

It is impossible not to consider that the tapetum will influence light reception and vision. First, light passing through the retina will be reflected by the tapetum so that the reflected light will be yellow. Second, the fluorescence maximum of riboflavin is 520 mμ at neutrality[8], and this fluorescence is maximally activated by light of 445, 370 and 266 mμ. Light of 445 and 370 mμ will penetrate the eye, be absorbed by the tapetum and re-emitted as light of 520 mμ, owing to the fluorescence of riboflavin. Dodt and Walther[13] find that the sensitivity of the light-adapted retina of the cat is much greater in the tapetal than in the non-tapetal area though there is no difference in the dark-adapted eye. Dodt[14] has also found that injection of fluorescein in the albino rabbit increases the sensitivity of the retina. If lemur eyes contain visual purple with an absorption maximum of 500 mμ and hence a visual sensitivity which is greatest to light of this wave-length, it should benefit an animal to have shorter wave light transformed into light of 520 mμ. The absorption by visual purple is 50 per cent maximal at 445 mμ and 90 per cent maximal at 520 mμ[15]. In both these ways —as a reflector, and as a fluorescing substance—riboflavin may therefore increase the stimulus received by the light-sensitive cells.

I wish to thank Dr. H. Davson for the gift of two lemurs (*Galago crassicaudatus*), Prof. R. T. Williams and Mr. Rosen for determining the fluorescence spectrum of the tapetal extract, Dr. H. H. le Riche for examining the tapetum spectrographically and Mr. Reading for help with ultra-violet microphotography.

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Gas Secretion in Coregonids

IT is known that the coregonids do not possess a counter-current system in the vascularization of the swim-bladder. In his classical work Hüfner[1] showed that *C. acronius* has a gas content in the swim-bladder consisting mainly of nitrogen—some 99 per cent. This was later verified by others[2–4] on *C. acronius* and related species.

Then the question arose whether this gas mixture is primarily secreted. All attempts by artificial stress to make coregonids secrete have hitherto been unsuccessful.

As reported previously[4] the Norwegian *C. lavaretus* was found to secrete oxygen. A single specimen of *C. acronius* caught by me in the Bodensee in May 1957 had an oxygen content of 30·8 per cent. Assuming that periods of secretion and non-secretion occur, the question is whether the former investigations had been performed in the period of non-secretion. A further investigation on *C. acronius*, the classical material of Hüfner, was therefore initiated in October. The fishes were caught at a possible secreting period. Ten specimens were caught near Unteruhldingen by gill nets at depths of 80–100 m. Flotation measurements of the fishes gave buoyancy depths of 81–120 m. All the specimens had an oxygen content ranging from 15·2 to 18·3 per cent. By mass-spectrometry the argon/nitrogen ratio was measured, giving values of 90·1–97·0 per cent of the air.

The relatively low oxygen content may indicate that the secreting period is terminated and the oxygen is being absorbed. The low argon content is in favour of this theory[4].

The same process has been shown by experiments by me to occur in a physoclist fish (*Gadus callarias*). The fish was over-inflated with a mixture of 23·4 per cent nitrogen and 73·7 per cent oxygen. After 4 days the fish showed normal buoyancy with a gas content in the swim-bladder consisting of 95·5 per cent nitrogen and 3·7 per cent oxygen.

The results obtained indicate that the problem of secretion is common for the physostome and physoclist fishes, and the lack of a counter-current system does not exclude oxygen secretion.

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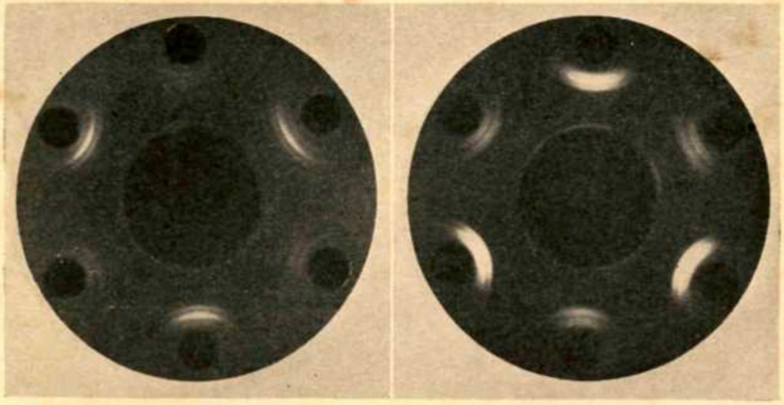
A Critical Test of Antigenic Relationships

A NEED has long existed for a simple, direct method for determining whether cross-reacting antigens are identical, or merely similar. Isolation and immunochemical characterization of individual antigens are often impossible. Measurement of precipitation or agglutinin titres, or of optimum proportions, are generally too crude to make distinction between identity and similarity possible, and may lead to confusing results[1]. Wodehouse[2] has reported the method of cross-neutralization to be unsuited for antigenic analysis of allergens.

Introduction of the immuno double-diffusion gel plate technique by Ouchterlony[3] apparently provided the required means for studying antigenic relationships. Complete fusing of precipitation bands of two antigens was taken to indicate antigen identity. Spur information was postulated, required and, in many cases, observed in antigen similarity without identity. Unfortunately, the conventional Ouchterlony technique can be deceptive. Its application has misled several investigators to postulate an identity of the major antigen(s) of the pollens of different species of grasses[4–6].

Re-investigation of grass pollen antigen relationships by a new agar gel technique has produced conclusive evidence of antigenic similarity rather than identity. The method is based on a modification of a pattern and technique published previously[7,8]. It is simple and permits analysis of complex antigen mixtures as well as isolated antigens.



(*a*) (*b*)

Fig. 1. Difference between precipitation band intensities of homospecific and cross-reacting heterospecific antigen/antibody systems. Outer wells contain, alternately, extracts of brome (*Bromus mollis*) and cocksfoot (*Dactylis glomerata*) pollens, starting with brome in top well. *a*, Antiserum to cocksfoot pollen in central well; *b*, antiserum to brome pollen in central well

Patterns are cut in the agar with an accurately tooled cutting instrument (obtainable from the Shandon Scientific Co., London, S.W.7). Two plates are used for the comparison of two antigen solutions. In the central well of one plate is placed 0·2 ml. antiserum to one of the antigen solutions. The other plate similarly receives the antiserum to the other solution. Antibody gradient is established in the agar by incubating the plates with the sera at 37° C. for 24–72 hr. Suitable concentrations of the two antigens are then placed in alternate circumferential wells in both plates and the plates incubated for a further 24 hr.

If the antigens are identical, the precipitation patterns at all wells are of equal intensity. Where a similarity without identity exists, alternate wells will show strong and weak precipitation band patterns, the positions being reversed in the two plates. In each plate the homospecific antigen gives strong bands, the related heterospecific antigen weak bands (Fig. 1).

The technique has been thoroughly tested on both complex and simple antigen systems. It has been found to be a critical and discriminating test of antigenic relationships. Extension of observations and theoretical considerations will be made the subject of a subsequent paper.

Photographs of the gel plates were made on the Lawson apparatus[9].

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PLANT PHYSIOLOGY

Copper–Cellulose Complexes

OUR attention has been directed to the fact that our recent paper[1] on the subject of timber preservation by copper compounds is being quoted in the literature[2] in support of the copper–cellulose hypothesis of Abrams and Bottoms[3].

These workers and their associates have concluded, largely from indirect evidence, that after treating wood or cellulose with a copper formate solution followed by autoclaving or heating, the copper is converted into a copper–cellulose complex and that this complex confers durability. This is known as the N.C.G. process, and its use has been advocated for wood, cotton and other cellulosic materials as a preservative measure.

During our examinations in the electron microscope[1,4] of wood treated with water-soluble preservatives or aqueous solutions of metal salts, characteristic electron diffraction patterns were noted which were interpreted as referring to metal–cellulose complexes in the wood. This interpretation was later confirmed[5,6], and the electron-diffraction diagrams were shown to arise from a two-dimensional array of metal atoms adsorbed on to the surface of cellulose microfibrils.

The properties of this metal–cellulose complex, however, do not appear to be consistent with the claims of Abrams and Bottoms. We have found that complexing takes place in the cold from aqueous solutions of copper salts so that no heat is necessary for the adsorption and, in addition, the electron diffraction pattern given by the complex remains unchanged after heat treatment. Cations from solutions of metal salts, other than those of copper, form a metal–cellulose complex so that the reaction is not restricted to copper formate solutions.

Abrams and Bottoms have claimed that N.C.G.-treated cellulose is resistant to hydrolysis and will not dissolve in concentrated hydrochloric acid, whereas we have found that, in the case of the complex detected by means of electron diffraction analysis, the 'bound' copper is instantly removed by dilute acids.

Thus, while our investigations have confirmed the existence of a metal–cellulose complex, the configuration of which has been elucidated by means of electron diffraction analysis, the general behaviour of this complex does not resemble that of the copper–cellulose complex postulated by Abrams and Bottoms, and our findings can in no way be taken to support their copper–cellulose hypothesis.

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Tetragonin : a Yeast Growth-regulating Substance from *Tetragonia expansa*

THE number of antimicrobial substances isolated from higher plants is small. Recently, studies with *Tetragonia expansa* or New Zealand spinach have shown it to contain a water-soluble component which we have tentatively named 'tetragonin'. Tetragonin is characterized by a narrow spectrum, being active apparently specifically upon *Saccharomyces* spp.

Activity tests were conducted with the agar diffusion paper disk method[1] using 1-day-old cultures of *Saccharomyces carlsbergensis* ATEE 9080 as test organism. The medium containing 2 per cent malt extract and 1 per cent agar, inoculated with approximately 5×10^7 cells/ml., was spread on glass plates in layers 1 mm. thick.

A preparation was purified by addition of chloroform to the centrifuged juice obtained from the stems of well-developed plants. The supernate was kept on a steam-bath for 10 min. and then centrifuged. The addition of one part ethanol to two parts of the supernate resulted again in precipitation. This supernate was dried at 50° C. and dissolved in methanol. After drying, a hygroscopic, yellow, sweet-smelling substance was obtained.

A methanolic solution of this partially purified substance was chromatographed on Whatman No. 1 filter paper. The dried chromatograms were placed on top of agar plates inoculated with *Saccharomyces carlsbergensis*. The R_F values thus obtained with 3 : 2 mixtures of methanol–water were 0·44–0·46, with 3 : 2 mixtures of ethanol–water 0·39–0·40 and of 3 : 2 mixtures of acetone–water 0·38–0·39. The same R_F values were obtained using the eluate of the chromatogram and also with the crude leaf juice. Tetragonin is very soluble in water, soluble in methanol, scarcely soluble in absolute ethanol and *iso*propanol, and insoluble in benzene, carbon tetrachloride, toluol and chloroform. The compound is stable at 100° C. for about 20 min., then undergoing decomposition. This decomposition with respect to time is logarithmic. The relationship between zone diameter and the logarithm of concentration is a straight line. Tetragonin dried on filter paper retains its activity for at least one year.

Tetragonin in high concentration inhibited, but in lower concentration stimulated, the multiplication also of several types of *Saccharomyces cerevisiae* and of *S. cerevisiae* var. *ellipsoideus*, in addition to *S. carlsbergensis*. No activity was observed with the following micro-organisms :

Yeasts : *Schizosaccharomyces octosporus*, *Endomyces magnusii*, *Sporobolomyces* sp., *Endomycopsis fibuliger*, *Rhodotorula gracilis*, *Torulopsis utilis*.
Bacteria : *Escherichia coli*, *Serratia marcescens*, *Bacillus subtilis*, *B. cereus*.
Actinomycetes : *Actinomyces roseus*, *Streptomyces floridae*, *Proactinomyces roseus*, *Nocardia grisea globispora*.
Phycomycetes : *Rhizopus nigricans*, *Mucor* sp.
Ascomycetes : *Aspergillus ruber*, *Penicillium striatum*.
Basidiomycetes : *Puccinia graminis*
Fungi Imperfecti : *Aspergillus niger*, *A. flavipes*, *Penicillium chrysogenum*, *P. notatum*, *Trichothecium roseum*, *Colletotrichum lini*, *Botrytis cinerea*, *Cercospora beticola*, *Pullularia pullulans*.

Tetragonin is present throughout the plants, and though its concentration varies considerably during the period of cultivation, it is always the highest in the roots. In the young plants the leaf juice shows higher activity than that of the stem, but as the plant ages, the activity of the stem becomes higher than the activity of the leaves, while the activity of the lower stem parts approaches that of the roots. Green unripe fruit show an activity between that of the leaves and stems. The aqueous extract of the dry ripe fruit showed no signs of activity.

These observations indicate a new antibiotic substance from a higher plant. That the antibiotic is very specific for *Saccharomyces* spp. may lead to industrial application. That the concentration in the plant roots is the highest may indicate an ecological role, a feature also indicated by the macrocounteractions observed in Nature.

These experiments were begun in the Plant Breeding Research Institute, Sopronhorpacs, Hungary, and were finished at the Universities of Wisconsin and Bologna.

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Separation of Anthocyanins from Plant Extracts

ALTHOUGH cellulose column chromatography[1] is generally useful for the separation of anthocyanin mixtures, difficulties may be encountered in applying this technique in the presence of large amounts of other flavonoid materials. Thus, in the case of complex petal extracts, overlapping of bands can occur so that the anthocyanins are contaminated with other pigments; and in the case of extracts containing mobile leuco-anthocyanins, the anthocyanin bands are located within a broad diffuse zone containing the former compounds. While these difficulties can be overcome by further purification involving partition between solvent systems, or repeated cellulose column chromatography, a very convenient and effective method is provided by preliminary treatment on a column of polyamide[2-4].

The general application of polyamide (powdered nylon) columns in the purification of flavonoids has already been reported[3,4], the separations achieved depending on two factors: the greater solubility of glycosides in water as compared with aglycones, and the strong absorptive capacity of the powdered nylon for hydrogen-bonding phenolic groups. Thus flavonoid glycosides can be separated from their aglycones by using aqueous methanol followed by anhydrous methanol for elution; but compounds of the same class cannot be separated from one another by this method. It seemed likely that using a combination of the two absorbents (cellulose favouring the retention of water-soluble compounds, polyamide the reverse) it would be possible to separate most mixtures of flavonoid compounds.

Preliminary investigations showed that anthocyanins and anthocyanidins are only slightly retained by polyamide columns, being readily eluted by the usual anthocyanin solvents providing they are sufficiently acid to prevent fading of the pigment. The upper layer of butanol – 2 N hydrochloric acid was found to be most suitable, and had the added advantage that the eluates could be applied directly to the cellulose column[1]. Addition of two parts by weight of 'Celite' to the polyamide hastened the movement of the solvent through the column and did not greatly diminish the absorptive properties of the polyamide.

The polyamide–'Celite' mixture was packed as a slurry in the solvent system and pressed firmly into the column to a uniform compactness using a closely fitting tamper. The pigment extracts were added as a strong solution in the solvent system, to which a little methanol was added if necessary to assist the solution of the difficultly soluble components. On development with aqueous acidic butanol both anthocyanidins and anthocyanins moved rapidly down the column as one band; most of the other flavonoids were more firmly held in this solvent system but could be separated if required by further elution with aqueous or absolute methanol[3,4]. Monomeric leuco-anthocyanins, however, were found to move off the column on continued elution with aqueous butanol, and this technique offers a method for the separation of anthocyanins from leuco-anthocyanins, superior to that previously published[5], in that both fractions are recoverable.

This technique has been applied successfully to extracts of *Dahlia* petals, *Streptocarpus* petals and cacao beans, anthocyanins being obtained free from other flavonoid compounds. Anthocyanidins from acid-treated leuco-anthocyanin solutions could also be obtained in a pure state using this method, accompanying polymeric material being absorbed firmly on the column[2].

Such polymeric material could not be completely removed from the column even by alkali washing, but in all other cases the polyamide, which is apparently not affected by the recommended solvent system, can be freed from absorbed compounds by washing with suitable solvents, and used again. It is to be hoped, however, that this extremely useful and potentially cheap absorbent will become so readily available that this will not be necessary.

We wish to thank Dr. D. E. Hathway, British Leather Manufacturers' Research Association, for a liberal supply of polyamide, and Dr. J. Harborne, John Innes Horticultural Institution, for a gift of pure anthocyanins.

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Effect of Coumarin on the Germination and Growth of Rice Seedlings

UNSATURATED lactones like coumarin, parasorbic acid, etc., came to prominence after the postulation of blastocholine, the group of unknown substances from the ripe fruits which were found to inhibit the germination of corn seeds. Work was further extended to study the physiological behaviour[1] as well as cytological effects[2] produced by these unsaturated lactones. Coumarin at high concentrations has been reported to have inhibitory effects in several plants[3-7]. The present investigation was designed to study the effect of coumarin (the lactone of *o*-hydroxy-*cis*-cinnamic acid) at various concentrations on the germination and growth of rice seedlings.

Graded seeds of the early variety of rice, *N.* 136, were soaked separately in the different concentrations, 0·5, 1, 5, 10, 100 and 1,000 parts per million of coumarin. Another set soaked in distilled water served as the controls. After 72 hr. soaking the seeds were thoroughly washed with distilled water and allowed to grow on moist filter paper in Petri dishes in the dark at room temperature. Three replications were maintained for each concentration. Six seedlings were taken at a time at random from each Petri dish, and readings were recorded at intervals on the length of the longest root, length of shoot, total fresh weight of all the roots and total fresh weight of the shoot.

The inhibitory effect of coumarin on the germination and growth of rice seedlings at high concentrations was very conspicuous. Seeds treated with 1,000 parts per million did not sprout at all, whereas the percentage of sprouting was almost the same as the controls in all other concentrations. Though the seeds treated with 100 parts per million sprouted as usual, their subsequent growth was very much adversely affected by this concentration. The radicle in this case emerged much later than the plumule and was marked with a conspicuous swelling of the hypocotyl. The initial inhibitory effect of this concentration, however, did not persist for long and rapidly diminished with the increase in the age of the seedlings. Lower concentrations behaved in a very different way. Much lower concentrations such as 0·5 and 1 parts per million produced significant accelerating effect on the growth of root as well as shoot. The maximum effect of 14·46 and 14·45 per cent increase in the length of the longest root and the shoot together with 63·27 and 29·12 per cent increase in fresh weights of all the roots and the shoot respectively over the controls was observed in the lowest concentration of 0·5 part per million.

With the increase in concentration to 5 parts per million a bifurcation in the effect of coumarin was observed in that the growth of the roots was inhibited while the growth of the shoot was still maintained on the accelerated side. With still further rise in concentration to 10 parts per million the inhibition of the growth of the roots was intensified and the direction of growth of shoot was reversed from that of promotion to inhibition. This onset of inhibitory effect simultaneously on both the roots and shoot which started at 10 parts per million persisted all through in the higher concentrations. The maximum effect of 56·56 and 36·31 per cent decrease in length of the longest root and the shoot together with 63·27 and 23·55 per cent decrease in fresh weights of all the roots and the shoot respectively in comparison with the controls was noted with 100 parts per million. Thus two things were marked from the behaviour of coumarin: (*a*) the ranges of concentration for acceleration of root and shoot growth are different, the optimum range of concentration for elongation of shoot being higher than that for root; (*b*) the accelerating effect was maximum at very low concentrations, with a gradual diminution of this effect with the rise in concentration and ultimately culminating in a reverse effect of inhibition beyond a certain stage at higher concentrations. Thus as has been observed for indoleacetic acid[8], roots and stems react in a comparable way to coumarin, their growth being inhibited by relatively high and promoted by relatively low concentrations.

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BIOCHEMISTRY

Reduction of Menadione in Hexane by Chlorophyll a under Ultra-violet Irradiation

WE have found that chlorophyll can reduce vitamin K upon illumination. This reaction can be followed by the loss of fluorescence induced by exposure of chlorophyll to light in the presence of vitamin K. This loss of fluorescence occurs at concentrations and intensities of illumination at which the fluorescence of chlorophyll alone does not vanish. The reduction of vitamin K to the hydroquinone form can be shown by reduction of 2,6-dichlorophenol-indophenol.

The following experiments illustrate this finding. 1·85 mμmoles of chlorophyll *a* were mixed with 5 μmoles of menadione (2-methylnaphthoquinone, vitamin K_3) in 5 ml. hexane. The characteristic red fluorescence of chlorophyll *a* appeared whenever this solution was illuminated by light of wave-length 365 mμ from an ordinary black light source. Prolonged illumination by this source caused the fluorescence to fade. This was apparent within 15 sec. and extinction of the fluorescence was complete within 5 min. The fluorescence did not reappear within 48 hr. A solution of chlorophyll at the same concentration, without menadione, was not bleached under these conditions, nor did its fluorescence fade.

One method of analysis of vitamin K is to titrate its reduced (hydroquinone) form with 2,6-dichlorophenol-indophenol[1]. This reduction decolorizes the blue dye. 1 ml. of an aqueous solution of the sodium salt of 2,6-dichlorophenol-indophenol (1·33 μmoles) was decolorized to about half the original intensity of its blue colour when shaken vigorously with a chlorophyll–menadione solution which had been illuminated half an hour previously. Further shaking under 365-mμ illumination decolorized the dye completely in about 5 min. Neither chlorophyll nor menadione separately was able to reduce 2,6-dichlorophenol-indophenol under these conditions, nor was the dye itself decolorized when illuminated and shaken with hexane. Menadione itself reduced the dye when illuminated ten times as long as sufficed for decolorization of the dye in the presence of both chlorophyll and menadione. The same results were obtained with de-aerated solutions under nitrogen. The blue colour of the dye could be brought back after decolorization by oxidation with a very dilute aqueous solution of iodine and potassium iodide.

A number of reactions have been demonstrated by these experiments. Excitation of chlorophyll[2,3]:

$$\text{Chl} + 2\,h\nu \rightarrow \text{Chl}^* \qquad (1)$$

Transfer of electrons to menadione (K_3):

$$2\,\text{Chl}^* + K_3 + 2\,H^+ \rightarrow 2\,\text{Chl}^+ + H_2K_3 \qquad (2)$$

Transfer of electrons to 2,6-dichlorophenol-indophenol (DCIP):

$$H_2K_3 + \text{DCIP} \rightarrow H_2\text{DCIP} + K_3 \qquad (3)$$

The concentrations used in our experiment were such that the chlorophyll had to turn over at least a thousand times for complete reduction of the dye to occur. Therefore, a follow-up reaction to (2) must occur in order to return Chl+ to its original form. Since this reaction occurs when an aqueous phase is added to the system, we believe that the follow-up reaction consists of the oxidation of water:

$$H_2O + 2\,\text{Chl}^+ \rightarrow 2\,\text{Chl} + 2\,H^+ + \tfrac{1}{2}\,O_2 \qquad (4)$$

The occurrence of reaction (4) still has to be established, however.

The reduction potentials[4] involved in these reactions are:

$$2\,H^+(10^{-7}M) + K_3 + 2e \rightarrow H_2K_3 \qquad E^0 = 0{\cdot}009\ \text{V.} \quad (5)$$

$$2\,H^+(10^{-7}M) + \text{DCIP} + 2e \rightarrow H_2\text{DCIP} \qquad E^0 = 0{\cdot}217\ \text{V.} \quad (6)$$

$$2\,H^+(10^{-7}M) + \tfrac{1}{2}\,O_2 + 2e \rightarrow H_2O \qquad E^0 = 0{\cdot}815\ \text{V.} \quad (7)$$

The potential of half-reaction (5) shows that the reduction of menadione uses radiant energy absorbed in reaction (1) as activation energy, but that no energy storage in a thermodynamic sense has taken place. Other vitamin K components or analogues have more negative reduction potentials, so that energy storage would occur even in a thermodynamic sense upon the reduction of these compounds. The reversal of half-reaction (7), which is involved in reaction (4), would indicate a considerable storage of energy in the course of the latter reaction.

We hope that the reactions reported here will prove helpful in studying the mechanism of photosynthesis as well as in converting the energy absorbed by chlorophyll into useful products. Work leading to further elucidation of these reactions is being continued.

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Determination of Molecular Weights of Polysaccharides by Over-oxidation with Periodate

IN addition to its capacity to oxidize α-glycol groups, periodate oxidizes C—H groups flanked by two α-carbonyl groups[1]. Such structures are exposed in the reducing-end units of 1 : 2-, 1 : 3- or 1 : 4-linked aldohexopyranose oligosaccharides when the α-glycol groups have been oxidized.

The requisite carbonyl groups for activation of the C—H bond are found as aldehyde groups. The oxidation of the C—H group creates new α-glycol centres and further oxidation (over-oxidation) ensues. The oligosaccharide is therefore slowly eroded from its reducing-end unit with the evolution of carbon dioxide from the carbon atom carrying the activated hydrogen. The reaction continues either until the molecule is completely converted into carbon dioxide, formic acid and formaldehyde, or until structures are encountered which are no longer over-oxidizable, for example 6-substituted monosaccharide units. This behaviour has previously been used for locating the position of 6-substitution in an oligosaccharide[2]. Another use of the over-oxidation reaction is in determination of degree of polymerization of an oligosaccharide, since the rate of over-oxidation is dependent on the content of reducing-end groups. When the laminaridextrins (1 : 3-linked β-glucose oligosaccharides)[3] were over-oxidized in unbuffered sodium metaperiodate at room temperature the rate of periodate uptake was found to be directly proportional to the reducing-end group content, and degree of polymerization of laminarin was determined by measuring its rate of over-oxidation in comparison with that of the laminaridextrins of known degrees of polymerization[4]. We have re-investigated this method in an attempt to reduce the period of measurement (> 100 hr.) and the amount of material required. The latter object was achieved by measuring the rate of liberation of formaldehyde with the sensitive chromotropic acid reagent[5]. The maltodextrins[6] (1 : 4-linked α-glucose oligosaccharides) were used as test substances.

In phosphate or bicarbonate buffer at neutral *p*H there was a marked increase in the rate of over-oxidation over that occurring in unbuffered periodate (*p*H 4); but the method was unsuitable because, in addition to the endwise erosion, a random breakdown of the polymers occurred. For example, Schardinger α-dextrin (*cyclo*hepta-amylose), which is non-reducing and should not yield any formaldehyde, produced 1·61 mol. prop. of aldehyde during 22½ hr. oxidation in phosphate buffer *p*H 7·0 at 23° C. Recourse was had to the use of acid media and in acetate-periodate *p*H 1·90 at 50° equimolar amounts of maltodextrins in the series maltose-maltopentaose were over-oxidized at exactly equal rates. The time of oxidation necessary for the accurate determination of the rate constant was only 2 hr. Synthetic amyloses of known average degree of polymerization[7] were then prepared and their rates of over-oxidation compared with those of the maltodextrins. The values of degree of polymerization of such amyloses determined by measurement of the rate of over-oxidation agree well with the known values of degree of polymerization of the amyloses (Table 1).

The amount of polysaccharide required for the estimation of degree of polymerization is about 1·5 mgm. and the period of measurement need not be more than 20 hr. With more material the period is

Table 1. DETERMINATION OF DEGREE OF POLYMERIZATION OF SYNTHETIC AMYLOSES

By synthesis*	By over-oxidation
20·1	21·5
36·4	36·6
43·7	42·3
53·7	52·4
68·7	70·1

* The amylose is synthesized by potato phosphorylase from glucose 1-phosphate and a known amount of pure maltodextrin primer. Measurement of inorganic phosphate liberated when the synthesis is terminated enables the increase in length of the primer to be calculated (ref. 7). In these experiments the primer was maltopentaose or maltopentaitol.

correspondingly less. The method probably cannot be applied to polysaccharides of degrees of polymerization of more than 100 since some depolymerization occurs in the acid medium used for the oxidation and the consequent error will increase as the degree of polymerization increases. At degrees of polymerization less than 100 the error proved to be negligible.

The method has been used in the determination of degrees of polymerization of other polysaccharides and oligosaccharides, and it is hoped to publish full details elsewhere.

We thank the Nuffield Foundation for a grant through Prof. W. T. J. Morgan to one of us (F. W. P.).

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Aerobic Fermentation of Whey by a Nitrogen-fixing Strain of *Aerobacter aerogenes*

DURING the course of investigations on the utilization of cheese whey by micro-organisms, a strain of *Aerobacter aerogenes* was found capable of growing in whey and increasing the total protein of the whey without requiring the addition of a fixed form of nitrogen. Various attempts to convert cheese whey into useful substances by microbiological means have been covered in the review by Wix and Woodbine[1]. Cheese whey is a waste product with a high potential energy source in the form of lactose which has been studied in this laboratory as a substrate for members of the genus *Azotobacter*[2]. This was concerned with increasing the protein content of whey by the production of bacterial cell material. *Azotobacter* will not use lactose. Since we found that hydrolysis of the lactose must be followed by the removal of salts and other toxic ingredients in order to support growth of *Azotobacter*, attention was directed to other micro-organisms. An economic advantage of the genus *Azotobacter* is its nitrogen-fixing ability. Hence, interest was turned to a nitrogen-fixing strain of *Aerobacter aerogenes* which was recently discovered in this laboratory[3]. Pirt[4] has shown that the efficiency of conversion of substrate carbon to cell carbon and carbon dioxide by *Aerobacter* is directly proportional to the degree of oxygenation of the culture. This indicated that fermentation of whey could be accomplished under aerobic conditions.

All fermentations reported here were carried out in New Brunswick Model *F*07 fermentors of 7·5-l. capacity. 5 l. of acid whey were neutralized with potassium hydroxide, added to a fermentor, and sterilized by autoclaving at 15 lb. pressure for 15 min. The fermentors were inoculated with young cultures of *Aerobacter aerogenes* 88, stirred at 320 r.p.m., and aerated at a rate of 10 l. of air per minute. The temperature of the fermentations averaged 30° C. Excessive foaming was controlled by the addition of 'Dowex *AF* Antifoam'. The fermentations were sampled periodically over their 6–12 day incubation periods. The suspended solids, including the cells, were removed by centrifugation, recovered by acetone trituration, and dried to constant weight. Microkjeldahl determinations were made for total nitrogen and were the basis of the protein values presented.

Analysis of a typical fermentation showed the protein of the liquid whey culture to be 10·9 gm./l. before fermentation and 15·7 gm./l. after 10 days, an increase of 4·8 gm./l., or 44 per cent. Interest was confined, however, to the centrifugable portions of the culture. The dry weight of this portion increased from 10 gm./l. at the outset to 13·7 gm./l. at the termination of 10 days incubation, an increase of 3·7 gm./l., or 37 per cent. The protein of the centrifugate was increased from 42·9 to 68·1 per cent during fermentation, an increase of 59 per cent. As indicated in Fig. 1, total nitrogen increased throughout the fermentation periods. These findings appear to indicate that some nitrogen fixation has occurred with aerobic cultural conditions. In this connexion, the report by Pengra and Wilson[5] shows a several-fold increase in cell nitrogen by growing *A. aerogenes* anaerobically, and adds that under their conditions

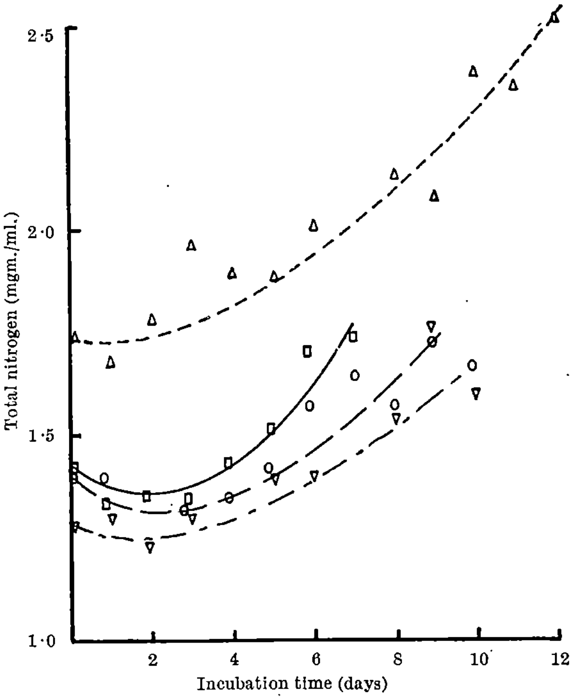

Fig. 1. Total nitrogen in four aerobic fermentations of whey by *A. aerogenes* 88 with incubation periods of 6–12 days. Each fermentation is with a different batch of cheese whey, which explains the difference in total nitrogen of the unfermented samples

their strains did not fix nitrogen aerobically. This is, of course, unlike the strain employed by Jensen[6], which fixed nitrogen equally well aerobically or anaerobically. One might also mention that Pirt[4] shows that in the presence of fixed nitrogen maximum conversion of carbohydrate to cell material occurs aerobically. Whereas Pengra and Wilson[5] employed a mineral salts and sucrose medium, Jensen[6] found a small amount of yeast extract or agar necessary. We were also unable to show nitrogen fixation unless whey or agar was present. This appears to suggest that a growth factor is required for aerobic nitrogen fixation by some strains of the genus *Aerobacter*.

This investigation was supported in part by a grant from the National Science Foundation.

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Amino-Acid Metabolism in Wool Roots

FOLLICLE material referred to as wool roots can be prepared in quantity from fresh sheep-skin by Ellis's method[1]. Each wool root consists of a bulb region, a pre-keratinization region and some fully keratinized fibre. Frequently, the inner root sheath is found to be attached to the wool root. Previous studies of homogenates of wool roots revealed the presence of several enzymes[2,3], some of which have been localized in hair follicles by histochemical methods[4,5]. Very little investigation of enzymes concerned with protein metabolism in the hair follicle has been made, despite the fact that protein synthesis is the major activity of this tissue.

The demonstration of free α-amino- and α-oxo-acids in wool roots led Ellis, Gillespie and Lindley[2] to suggest that enzymes could be present which participate in the tricarboxylic acid cycle as well as in transamination reactions. In the present work transaminase activity has been demonstrated. In addition it has been found that another enzyme commonly found in tissues actively engaged in protein synthesis is present, namely, transpeptidase[6,7].

A homogenate was prepared by macerating 5 gm. wool roots with 50 ml. water in a Waring blendor, filtering through coarse 'Terylene' cloth, centrifuging at 2,000g and dialysing the supernatant against 0·02 M phosphate buffer pH 7·4 overnight at +2° C. The supernatant was more satisfactory to use than the original homogenate because of the difficulty of removing the endogenous amino acids from the latter.

The systems used were:

(*a*) For transamination: 0·7 ml. reaction mixture containing 0·5 ml. extract or 0·02 M phosphate buffer pH 7·4, 5 μgm. pyridoxal phosphate, 20 μmoles α-oxo-acid and 20 μmoles L-amino-acid; incubated for 2 hr. at 37° C.

(*b*) For transpeptidation: 0·6 ml. reaction mixture containing 0·5 ml. extract or 0·02 M phosphate buffer pH 7·4, 20 μmoles amino-acid (or water), and 2 μmoles neutralized glutathione; incubated for 30 min. at 30° C.

(*c*) For citrulline iminase: (1) 1·0 ml. reaction mixture containing 0·5 ml. extract, 5 μgm. pyridoxal phosphate, 0·02 M potassium dihydrogen phosphate, 15 μmoles L-citrulline, 20 μmoles magnesium chloride, 5 μmoles neutralized adenosine triphosphate, and 2 μmoles ammonium chloride; incubated for 30 min. at 37° C.; (2) as (1) with 0·05 M borate instead of potassium dihydrogen phosphate and 15 μmoles L-arginine instead of L-citrulline and without ammonium chloride.

Following incubation, the reactions were stopped by the addition of 1 ml. warm ethanol; in (*b*) the ethanol contained 2·2 μmoles N-ethyl maleimide. The clear supernatants were dried *in vacuo* and then applied to Whatman No. 1 paper; samples (*a*) and (*c*) were developed in 80 per cent aqueous phenol, and (*b*) in 80 per cent aqueous *n*-propanol for 24 and 240 hr. respectively.

So far it has been possible to demonstrate the formation of alanine from pyruvic and aspartic acids, and glutamic acid from α-oxoglutaric acid and alanine or citrulline. It is of interest that citrulline, which occurs in the free state in wool roots[8] as well as combined in the inner root sheath[9], participates in transamination.

It was not possible to obtain evidence of citrulline iminase activity[10]. This enzyme catalyses the reversible conversion of citrulline to arginine and has been suggested as a possible constituent of hair follicles[11].

Evidence for the presence of γ-glutamyl transferase activity[6,7] in wool root homogenates was found by the demonstration of the formation of γ-glutamyl glycine from glutathione and glycine. It is perhaps significant that Haurowitz *et al.*[12] have recently provided evidence for the occurrence of γ-glutamyl residues in wool and the present finding of transpeptidase activity could have relevance to their formation. In addition to transpeptidation, the chromatograms indicated that wool roots probably also possess peptidase and/or protease activity, although cysteinyl–glycinase[13] activity was weak or absent. This enzyme is usually found in conjunction with transpeptidase activity.

We wish to thank Dr. F. J. R. Hird for a gift of adenosine triphosphate, glutathione and α-oxoglutaric acid, Dr. A. W. Rodwell for pyridoxal phosphate and Miss C. M. M. Mackinnon for technical assistance.

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Role of Lysine in catalysing Ester Hydrolysis

Recently, Gero and Withrow[1] have cited the catalysis of alkaline triglyceride hydrolysis by lysine as a chemical model of a biological reaction. They postulated a bifunctional[2] attack by lysine upon the carbonyl O and C of the ester linkage as the mechanism of this hydrolysis.

We believe that some objections can be made to their arguments for this mechanism. They have stated, "It stands to reason that the hydrogen bonds which the ε-ammonium group is to form with the carboxyl group of lysine and the O of the ester should be strongest when the N does not hold its hydrogens too tightly, because that is when they will be most readily donated for a hydrogen bond. Such would be the case just below the *p*H at which the ε-ammonium group of lysine loses a hydrogen and its positive charge. That happens at *p*H 9·5, so that lysine should be maximally active as a catalyst for ester hydrolysis around *p*H 8–9". The authors are clearly implying that N—H bond-strength is a function of *p*H. This, of course, is not the case. Instead, since they are describing the competition of several bases for protons, one would expect the usual arguments for acid-base equilibria to be applicable. In this case they are:

$$K_1 = \frac{[\epsilon NH_2]\ [R\text{—}\overset{\oplus OH}{\overset{\|}{C}}\text{—}OR']}{[\text{—}NH_3\oplus]\ [R\text{—}\overset{O}{\overset{\|}{C}}\text{—}OR']}$$

$$K_2 = \frac{[R\text{—}\overset{\oplus OH}{\overset{\|}{C}}\text{—}OR']}{[H\oplus]\ [R\text{—}\overset{O}{\overset{\|}{C}}\text{—}OR']}$$

$$K_3 = \frac{[\epsilon NH_2]\ [H\oplus]}{[\epsilon NH_3\oplus]}$$

Since K_3 has a value of $10^{-10\cdot53}$ for lysine[3] and K_2 should be about $10^{6\cdot0}$, depending upon the nature of the substituents of the carbonyl group[4], the concentration of the reacting species, $\text{—}NH_3+$ and $R\text{—}\overset{O}{\overset{\|}{C}}\text{—}OR'$, in the first equilibrium should be maximal and independent of *p*H over at least the *p*H range 4·0–9·5. Below the former *p*H the rate of ordinary acid hydrolysis and the protonation of the lysine carboxyl group would have to be taken into consideration. Consequently, the rate of the hydrolysis catalysed by lysine should be maximal and constant over this *p*H range. Inspection of their results does not show this to be the case. Instead the decrease of the hydrolysis rate with decreasing alkalinity below *p*H 8·6 is seen to follow closely the expected protonation of the α-amino group.

A further objection can be made to their choice of *p*H 8–9 as the range of maximal catalysis. The ε-ammonium group would not be expected to be appreciably dissociated below *p*H 9·5 since its *pK*$_A$ is 10·53. Catalysis then should not fall off below *p*H 9·0. Again, their results do not show this to be true.

Therefore it seems more likely to us that this is an example of general base catalysis similar to that reported for the imidazole group[5]. That is, the picture of bifunctional catalysis shown in Fig. 1 would be predicted.

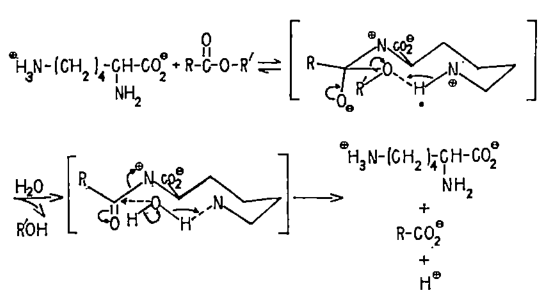

Fig. 1

An alternative to the second intermediate would be the co-ordination of a hydroxyl group by the ε-amino group into a position favouring its attack upon the carbonyl C. However, there is little to choose between the two possibilities.

Lysine as a ring structure as postulated by Gero and Withrow is sterically less suitable as a catalyst in this reaction sequence than it is in an open-chain form. Assumption of such a ring structure would be possible only with dissociation and loss of positive charge by the α-amino group, since it would otherwise require apposition of the two positive poles in the molecule. Consequently, the catalytic ability of lysine should decrease as the possibility for formation of ring structure increases above *p*H 8·95, the *pK*$_A$ of the α-amino group[3]. This is precisely what Gero and Withrow observed.

Consideration of the reaction sequence postulated above suggests that lysine should be very reactive with aldoses (in the hemiacetal configuration) since it is in good agreement with the mechanism deduced[6] for the Maillard reaction of amino-acids with aldoses. Inspection of the literature[7-9] shows that lysine is indeed particularly reactive with aldoses over the expected *p*H range, 7·0–9·5.

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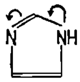
In their criticism of our paper[1], Chesbro and Hedrick make some points that are indeed well taken. Their objection to the implication that bond-strength is a function of *p*H is undoubtedly valid. However, the statement they quote from our paper does not imply such a functional relationship. Rather, we had in mind the stretching of the N—H bond which may be expected to occur before the bond breaks (more so the more alkaline the environment) and which certainly will allow the proton to function more effectively as an acidic catalyst. It is regretted that for the sake of brevity we were not explicit enough to forestall a mistaken implication.

Chesbro and Hedrick's objections to our writing of lysine as a chelate ring and their alternative mechanism for lysine-catalysed ester hydrolysis strike us as less convincing. They state that a hydrogen bond between the carboxyl group and the ε-amino group of lysine can be formed "only with dissociation and loss of positive charge by the α-amino group, since it would otherwise require apposition of the two positive poles in the molecule". It is not apparent where the apposition of two positive poles occurs when in the chelate structure the two poles are separated by a chain of three atoms, one of them a negatively charged oxygen atom. As to their catalytic mechanism, which is an adaptation of the mechanism proposed by Bender and Turnquest[2] for ester hydrolysis catalysed by imidazole, it must be observed that in Bender's mechanism imidazole functions as a basic catalyst by virtue of the electron richness of its tertiary nitrogen :



Whether the reasoning based on the catalytic potency of the tertiary nitrogen in imidazole can be fitted without further ado to the α-amino group of an amino-acid, even with the auxiliary role which Chesbro and Hedrick assign to the ε-amino group, remains to be seen. Certainly, if their reasoning is correct, there should be at least some catalysis even by a simple amino-acid such as glycine, and this we found not to be the case. Also, if we are dealing, as Chesbro and Hedrick suggest, simply with general base catalysis similar to that reported for the imidazole group, one would expect histidine, which contains both an α-amino group and an imidazole ring, to be a more potent catalyst of ester hydrolysis than lysine. As reported in our communication, we found the reverse to be the case.

However, it is probably of minor importance which particular mechanism will eventually be accepted to interpret our findings. It is significant, in my view, that on general chemical grounds a prediction was made regarding a biological reaction and that the prediction was verified by experiment.

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Synthesis of Adenylosuccinic Acid in Preparations of Mammalian Skeletal Muscle

FROM the observation that the nitrogen-15 of labelled ammonium citrate administered to rats appears in the 6–NH_2 group of the muscle adenine nucleotides, Kalckar and Rittenberg[1] have concluded that the nucleotides take part in very rapid reversible de-amination reactions. That ammonium citrate nitrogen is similarly incorporated into rabbit skeletal muscle has been confirmed by Newton and Perry[2]. They have further demonstrated that aspartic acid is a more active donor of the 6–NH_2 group and that the enzymic activity is concentrated in the sarcoplasmic fraction of muscle.

Although the rapid reactions involved in the dephosphorylation and subsequent de-amination of adenine nucleotides to inosine nucleotides in muscle have been well established[3], little is known concerning the processes whereby the inosine nucleotides are re-aminated. The re-amination of inosine monophosphate by its condensation with aspartic acid to form adenylosuccinic acid occurs in preparations of rabbit bone marrow, whereas in muscle extracts an accumulation of adenine nucleotides has been reported to occur in the presence of inosine monophosphate with either aspartic acid[2] or creatine[4]. Although adenosine monophosphate, together with fumaric acid, is formed from the splitting of adenylosuccinic acid in water-soluble extracts of *Escherichia coli*, strain *B*[5], it is unlikely that in muscle the adenine nucleotides are resynthesized in this manner. The product of this reaction, adenosine monophosphate, has not been identified in skeletal muscle, and if formed, would be lost to the adenine nucleotide pool by its rapid and irreversible de-amination to inosine monophosphate by muscle adenosine monophosphate deaminase[6–8].

In the present work, adenylosuccinic acid was found to be formed from inosine monophosphate and aspartic acid in extracts of acetone-dried powder of the water-soluble fraction of rabbit and beef skeletal muscle. The reaction requires the presence of guanosine triphosphate, a very low concentration of which (0·01–0·02 m*M*), together with adenosine triphosphate (5 m*M*), is effective in causing the condensation, although adenosine triphosphate alone is not. During the course of the reaction adenosine triphosphate breaks down to the diphosphate apparently by rephosphorylating guanosine diphosphate—in the presence of a nucleoside diphosphate phosphokinase—to guanosine triphosphate, the splitting of which supplies the necessary free energy for the formation of adenylosuccinic acid. If adenosine triphosphate is used to rephosphorylate guanosine diphosphate formed during the reaction, 50–55 per cent of the inosine monophosphate is converted to adenylosuccinic acid. If traces of both guanosine triphosphate and adenosine triphosphate are used, in the presence of a glycolysing system for regenerating the latter from adenosine diphosphate, 90–100 per cent condensation of inosine monophosphate with aspartic acid is attained after 3-hr. incubation at 37°.

Fig. 1 shows the formation of adenylosuccinic acid in both undialysed and well-dialysed (2 days against 0·04 *M* potassium chloride) extracts of acetone-dried powder of rabbit skeletal muscle, in a reaction mixture containing 6 m*M* aspartic acid, 2·5 m*M* inosine monophosphate, 3 m*M* magnesium chloride, 4 m*M* fructose-1 : 6-diphosphate, 0·2 m*M* diphosphopyridine nucleotide, 50 m*M*, *p*H 6·9 glyoxaline buffer and 0·7 per cent protein solution. The course of the reaction was followed from the spectral change occurring as inosine monophosphate ($\lambda_{max.}$, 248 mμ) is converted to adenylosuccinic acid ($\lambda_{max.}$, 267 mμ). The triphosphates of uridine, cytidine, inosine (0·09 m*M*), and of adenosine (0·2 m*M*) could not replace the requirement for guanosine triphosphate, which increases the enzymic activity of the dialysed extracts to that of the undialysed extracts. The guanosine triphosphate is bound presumably to the enzyme causing the condensation, and is only released on exhaustive and prolonged

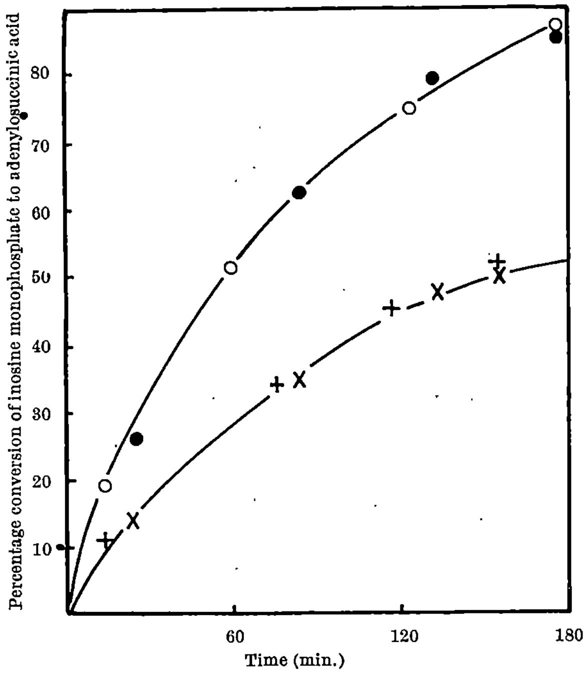

Fig. 1. The formation of adenylosuccinic acid from inosine monophosphate and aspartic acid, in undialysed extracts of rabbit muscle acetone-dried powder containing 0·005 mM adenosine triphosphate (●—●), in dialysed extracts containing 0·09 mM guanosine triphosphate and 0·005 mM adenosine triphosphate (○—○), in dialysed extracts containing 0·2 mM adenosine triphosphate (+—+) and in dialysed extracts containing 0·005 mM adenosine triphosphate with and without the triphosphates (0·09 mM) of uridine cytidine or inosine (×—×)

dialysis against 0·04 M potassium chloride at 0° for 8 days, by which time the enzymic activity is reduced by as much as 90 per cent. If such preparations are incubated with guanosine triphosphate and magnesium ions, and are then further dialysed for sufficient time to remove unbound guanosine triphosphate and magnesium, the activity is considerably greater than if the incubation before dialysis is carried out with guanosine triphosphate alone. The binding is apparently in the form of a complex of the enzyme, magnesium and guanosine triphosphate, in which form the enzyme is active.

The pH optimum of the condensation reaction is between pH 6·9 and 7·0. Inorganic phosphate in concentrations greater than 10 mM partially inhibits the reaction.

The significance of the adenine nucleotide de-aminating and re-aminating reactions in muscle is not known. If, as Kalckar and Rittenberg have suggested[1], the rates of these reactions increase with increase in muscular activity, it is possible that they play an important part in the process of muscular contraction.

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Identification of 10-Hydroxy-Δ^2-decenoic Acid in Royal Jelly

Royal jelly[1] is the sole food administered by young workers or nurse bees of the common honey bee species *Apis mellifica* to female larvæ destined to become queens. Larvæ destined to become drones (males) or workers (sexually undeveloped females) receive royal jelly during the first three days of their existence only and then a different food. The components of royal jelly responsible for its remarkable properties remain unidentified.

Townsend and Lucas[2] recognized and Abbot and French[3] confirmed that an optically inactive acid $A(C_{10}H_{18}O_3)$ comprised the major portion of the ether-soluble fraction of royal jelly. We have identified A as 10-hydroxy-Δ^2-decenoic acid; royal jelly is the only known source of this compound. The acid A (m.p. 52° C. (found—C, 64·6; H, 9·4 per cent; equiv. wt., 187·9: calc. for $C_{10}H_{18}O_3$—C, 64·5; H, 9·7 per cent; equiv. wt. 186)) comprises approximately 70 per cent of the ether-soluble fraction and approximately 15 per cent of royal jelly. The infra-red spectrum (melt on rock salt) of A showed $\nu_{max.}$ at 3,480 cm.$^{-1}$ (hydroxyl), 1,710 cm.$^{-1}$ (carboxylic acid) and 1,667 cm.$^{-1}$ (unsaturation). Platinum catalysed[4] hydrogenation of A indicated the presence of one double bond and afforded 10-hydroxy-decanoic acid, m.p. 74° (found—C, 64·1; H, 10·9 per cent: calc. for $C_{10}H_{20}O_3$—C, 63·8; H, 10·7 per cent); Chuit and Hausser[5] quote a melting point of 75–76° for this acid. The identity of the saturated acid was confirmed by conversion to sebacic acid on permanganate oxidation and the linearity of the carbon chain in A thereby established.

The presence of $\alpha\beta$-unsaturation in A, indicated by strong end absorption in the ultra-violet was confirmed as follows. Oxidation of A with the periodate–permanganate reagent[6] which cleaves double bonds, gave suberic acid, but oxalic acid, the anticipated second reaction product, could not be detected; under the same reaction conditions, *trans*-crotonic acid gave oxalic acid. Hydroxylation[7] of A with osmium tetroxide gave a product B shown by paper chromatography[8] and ionophoresis[9] to contain a single component in addition to some starting material. Oxidation of B with the periodate permanganate reagent[5] gave oxalic acid as did D-tartaric acid, *meso*-tartaric acid and *erythro*-2 : 3-dihydroxybutyric acid. Reaction of B with periodic acid directly on Whatman No. 1 paper followed by chromatographic separation of the products gave glyoxylic acid identified as its 2 : 4-dinitrophenylhydrazone (m.p. 194–196° decomp.) after elution from the paper. When the preceding experiments were essentially complete, our attention was directed to a report by Butenandt and Rembold[10] identifying A as 10-hydroxy-Δ^2-decenoic acid. No chemical proof of $\alpha\beta$-unsaturation or olefinic configuration was presented.

The olefinic C—H out of plane bending in *trans*-compounds is characterized[11] by strong absorption near 980 cm.$^{-1}$ in the infra-red. Both A and 10-hydroxy-decanoic acid absorbed near this value (987 and 981 cm.$^{-1}$ respectively) probably due to C—O stretching. Sheppard and Simpson[12] have observed a strong absorption in the range 675–725 cm.$^{-1}$ for a series of *cis*-olefins; but Allan, Meakins and Whiting[11] have assigned the absorption near 820 cm.$^{-1}$ to the olefinic C—H out of plane bending in *cis*-$\alpha\beta$-unsaturated acids and esters. A and its methyl ester show moderately strong absorption in the range 675–725 cm.$^{-1}$ whereas 10-hydroxy-decanoic acid does not. However, *trans*-crotonic acid and its methyl ester also absorb in this range. While the methyl ester of *A* shows no absorption near 820 cm.$^{-1}$ both *A* and 10-hydroxy-decanoic acid show weak absorption at 817 and 823 cm.$^{-1}$ respectively. Thus, on this basis, the configuration of the olefinic linkage in *A* cannot be allocated with certainty.

The biological origin of 10-hydroxy-Δ^2-decenoic acid has not been established. It is not present in the free state in nectar (collected from the hive), honey, or pollen of a representative monocotyledon (*Zea mays*), dicotyledon (*Alnus glutinosa*) and conifer (*Pinus montana*). The acid may be present in combined form or it may be a specific bee product.

10-Hydroxy-Δ^2-decenoic acid showed little activity against a representative range of bacteria and fungi; weak activity against strains of *Streptococcus pyogenes* and *Tricophyton rubrum* was displayed.

We thank Prof. M. Stacey for his interest in this work and Messrs. Glaxo, Ltd., for the biological activity assays.

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Effect of Reduced Diphosphopyridine Nucleotide on the Swelling of Isolated Mitochondria

It has been repeatedly reported that isolated mitochondria maintain a low water content if incubated in conditions favourable to oxidative phosphorylation[1–5]. Di Sabato and Fonnesu[6,7] found that this happens only when certain metabolites are used as the oxidizable substrate, for example, succinate, α-ketoglutarate and glutamate.

This communication deals with a study on the effect of reduced diphosphopyridine nucleotide on the swelling of the mitochondria in both conditions favourable and unfavourable to oxidative phosphorylation.

The preparation and incubation of mitochondria from rat liver, and the estimation of the swelling by the optical method were carried out as already described[6,7], with the difference that the readings of optical density were taken at 950 mμ. In order to establish whether reduced diphosphopyridine nucleotide is oxidized or not, soon after every reading at 950 mμ, the optical density of the mitochondrial suspension was measured at 340 mμ.

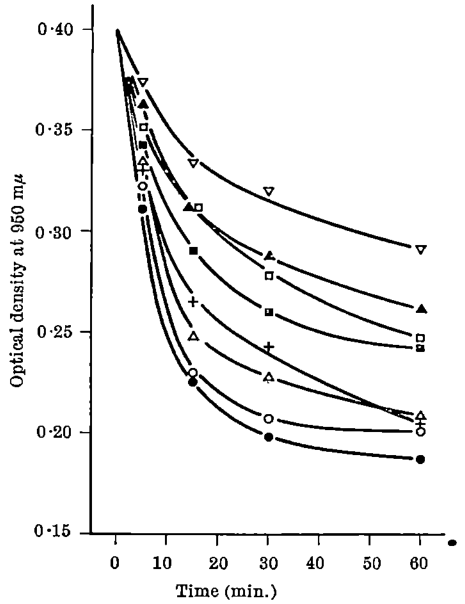

Fig. 1. Effect on mitochondrial swelling of various added substances: (1) +, control; (2) △, reduced diphosphopyridine nucleotide; (3) ○, cytochrome *c*; (4), ●, (2) + (3); (5) ▲, (2) + adenosine monophosphate; (6) ■, (5) + (3); (7) □, (3) + adenosine monophosphate; (8) ▽, (5) + 2,4-dinitrophenol

The composition of the standard incubation medium employed was as follows: magnesium sulphate, 30 μmoles; potassium phosphate buffer, *p*H 7·2, 60 μmoles; sucrose, 690 μmoles. The additions (Fig. 1) were: adenosine-5′-monophosphate, 180 μmoles; reduced diphosphopyridine nucleotide (Sigma Chemical Co.; 90–95 per cent purity), 6 μmoles; cytochrome *c*, 0·06 μmole; 2,4-dinitrophenol, 0·6 μmole; oxidized diphosphopyridine nucleotide, 6 μmoles. The final volume, after the addition of the mitochondria, was 6 ml.

Fig. 1 shows the rate of the mitochondrial swelling in the presence of various added substances. It is apparent that reduced diphosphopyridine nucleotide alone slightly enhances the 'spontaneous' swelling of mitochondria, but, at the end of the incubation, the swelling is nearly the same as that in the control. One can also see that cytochrome *c* alone enhances the mitochondrial swelling a little more than reduced diphosphopyridine nucleotide. When the mitochondria are incubated in the presence of both these substances, the swelling is greater than in the presence of either of them separately. When the mitochondria are incubated in conditions favourable to oxidative phosphorylation, that is, in media containing reduced diphosphopyridine nucleotide and adenosine monophosphate or these substances together with cytochrome *c*, the spontaneous swelling is partially prevented. This phenomenon, however, seems to be due to the action of adenosine monophosphate, since it was also observed with cytochrome *c* + adenosine monophosphate, as well as with adenosine monophosphate alone (not shown in Fig. 1; see refs. 7 and 8). That the protection from swelling in a system containing diphosphopyridine nucleotide and adenosine monophosphate is not due to the phosphorylation-coupled oxidation of the nucleotide, is also shown by the fact that the swelling is prevented rather than enhanced by the addition of 2,4-dinitrophenol.

Estimation of reduced diphosphopyridine nucleotide during the incubation showed that, in the absence of cytochrome *c*, almost 70 per cent of that added is oxidized in the first 30 min. The added cytochrome *c* enhances the rate of oxidation only slightly; on the other hand, greater amounts of cytochrome *c* have not been used, since, as reported above, this substance promotes mitochrondrial swelling.

In an attempt to elucidate whether the behaviour of the mitochondria is due to the oxidized diphosphopyridine nucleotide that is formed, experiments were carried out using the oxidized in place of the reduced form. The results of these experiments, not reported fully here for the sake of brevity, showed that the oxidized form is almost without effect on the mitochondrial swelling.

The most important fact arising from these experiments is that mitochondria are better protected from swelling in a medium unfavourable to oxidative phosphorylation than in one favourable to oxidative phosphorylation. This confirms once more that high-energy phosphate bonds are not essential for maintaining the mitochondria in the contracted state.

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Differences in Cyst(e)ine Content between Vegetative Cells and Spores of *Bacillus cereus* and *Bacillus megaterium*

IN the course of investigations on the role of sulphur amino-acids in the sporulation process of bacilli we studied the inhibitory effect of a large excess of cystine (10^{-4} *M*) on spore formation in *Bacillus megaterium*[1], and the incorporation of cystine-^{35}S and methionine-^{35}S, added in small quantities to the nutrient medium before sporulation, into sporulating cells of inhibited and of control culture[2]. The control culture, which was pre-adapted to cystine and treated with cystine just before sporulation, during sporulation incorporated considerable quantities of ^{35}S-amino-acids added at the time to the nutrient medium. During the 'cystine inhibition' the spore formation of *B. megaterium* remained for a long time in the first stage and the incorporation of labelled amino-acids was markedly lower.

Cultivating *B. megaterium* in the presence of ^{35}S-amino-acids from inoculation, we found that the free spores contained significantly more radioactive sulphur than the vegetative cells before spore formation[2]. With regard to the possibility of different cyst(e)ine contents of the vegetative cells and of spores we started to investigate these differences in both forms of bacilli.

A strain of *Bacillus cereus* (N.C.I.B. 8122) and our laboratory strain of *Bacillus megaterium* were used. Either bacillus was cultivated on a shaker at 30° C. in a liquid medium containing tryptic casein hydrolysate, 0·3 per cent; glucose, 0·1 per cent; phosphates and traces of some important ions. Cystine was added to the medium to give a concentration of 10^{-4} *M* before inoculation. The cells were harvested in order to estimate the cyst(e)ine after 12 hr. of cultivation, that is, about 2 hr. before spore formation; and after 100 hr. of cultivation, after complete liberation of spores and autolysis of the debris of sporangia. The harvested cells were killed with 10 per cent trichloracetic acid, washed, extracted with ethanol–ether (3 : 1) and heated in 5 per cent trichloracetic acid at 90° C. for 30 min. The precipitate, the fraction insoluble in hot trichloracetic acid, obtained in this way was used for the determination of cyst(e)ine content.

For the estimation of cyst(e)ine a specific method developed by Akabori[3] was used, involving reductive decomposition of proteins by hydrazine at 120° C. Hydrogen sulphide produced from both cystine and cysteine is driven out by acidification of the hydrazine with sulphuric acid and absorbed in zinc acetate solution. The zinc sulphide is estimated by the Carius method using dimethyl-*p*-phenylenediamine[4]. The nitrogen content of the precipitate was determined by the usual Kjeldahl method.

The results shown in Fig. 1 indicate that the spores of *Bacillus cereus* and *Bacillus megaterium* contain significantly more cyst(e)ine (about five times) than the vegetative cells before spore formation. This supports the hypothesis that the protein structure of spores differs substantially from that of vegetative cells. It is known that cystine, with its SS-bridges, plays an important part in the structure of some highly inert proteins, for example, keratins. A possible analogy with the structure of spores cannot be excluded. Stabilization of their protein structure

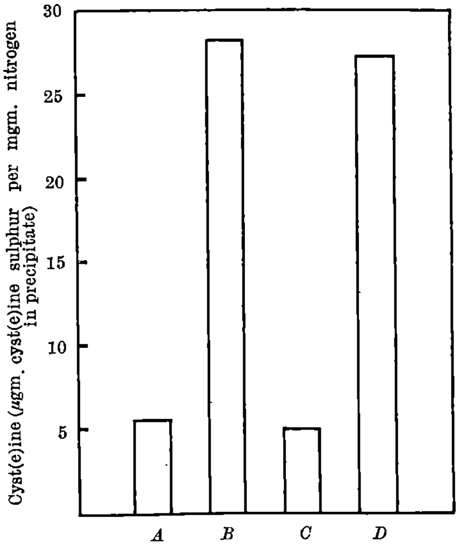

Fig. 1. The cyst(e)ine content of vegetative cells and of spores of *Bacillus megaterium* and *Bacillus cereus*. *A*, Vegetative cells; *B*, free spores of *B. megaterium*; *C*, vegetative cells; *D*, free spores of *B. cereus*

by SS-bridges may be a further mechanism contributing to the resistance of resting spores. Further details of the participation of cystine in spore formation will be described elsewhere.

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PHYSICAL SCIENCES

Thin Magnetic Films

THE preparation of thin films of magnetic alloys with specific characteristics is generally acknowledged to be a difficult task, owing to the large number of parameters involved. One such parameter, that of film thickness, might be expected to have a large effect on magnetic characteristics. The relation between this and coercivity has been studied theoretically by L. Néel[1], for film thicknesses in excess of domain wall thickness. For this condition, small variations in the thickness of the layer give rise to energy changes as domain walls are moved and lead to the relation $H_c \propto t^{-4/3}$, where H_c is the coercivity and t the average thickness. Tiller and Clark[2] have found $H_c \propto t^{-1}$ experimentally for t varying from about 250 A. to nearly 2,800 A.

To investigate this dependence more fully, an apparatus (Fig. 1) has been developed which allows the low-frequency hysteresis loop to be monitored both during deposition of the film and afterwards. The base, 1, on to which the magnetic alloy, 2, is to be evaporated is supported at the top of a flat-topped bell-jar, 3, The alloy is heated by induction from the coil, 4, and a shutter, 5, stops deposition on to the base, 1, until the alloy is evaporating freely. A Helmholtz coil, 6, produces an alternating aligning field of approximately 30 oersteds in the plane of the base, 1. Frequencies up to 1,000 c./s. have been tried, but generally 50 c./s. is used. The sensing coil, 7, consists of two rectangular windings each of 1,800 turns, with dimensions 2 in. × 1 in. The windings are connected so that the flux linkages with the evaporated specimen are additive, and are each adjusted slightly from the horizontal plane, so that the total flux linkage with the alternating aligning field is zero. Usually a small voltage is induced into the sensing coil from 50 c./s. eddy currents in metal components of the assembly and this requires separate cancellation. The output voltage from the sensing coil is thus proportional to $\dot{\varphi}$, where φ is the flux in the magnetic layer. The voltage is integrated and amplified, and a vertical deflexion proportional to φ is presented on an oscilloscope tube. The horizontal deflexion is derived by conventional means from the alternating current flowing in the Helmholtz coil. The base, 1, has generally been maintained at an elevated temperature during deposition by means of toroidally wound d.c. heaters, 8, applied to the outside of the bell jar, the magnetic field from which is negligible. The sensitivity of the apparatus as described is such that a recognizable hysteresis loop is obtained when the thickness of the layer is about 150 A., and no attempt has been made to improve upon this figure, so far.

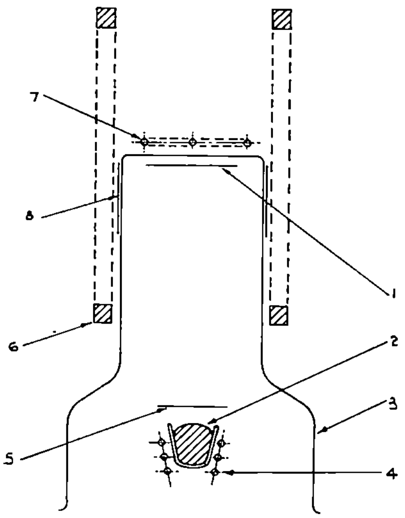

Fig. 1

Nearly two hundred evaporations have been made using the apparatus, the majority using lime soda glass for the base, 1. Substratum temperatures have ranged from 250° to 400° C., and alloy compositions from 75 per cent nickel, 25 per cent iron to 85 per cent nickel, 15 per cent iron. In the great majority of evaporations the coercivity changes little as the thickness varies from 150 A. to 1,500 A. If the evaporation is then continued up to 10,000 A., either a steady decrease of coercivity from its initial value of 1–2 oersteds to about 0·5 oersted is seen, or a sudden increase to 10–20 oersteds occurs at a thickness of about 2,000 A. The rapid increase in coercivity appears to be associated with atomic arrangement within the layer, since it continues for several seconds if the vapour stream is terminated during the increase with the shutter, 5. Moreover, the coercivity of such a layer can be reduced to 1–2 oersteds by annealing at 350–400° C. in a magnetic field. Occasionally, the coercivity first seen is in the region of 10 oersteds, decreasing to 1 or 2 oersteds at a thickness of about 300 A., and thereafter remaining constant up to about 1,500 A. Very rarely the coercivity has been seen to increase slightly as the thickness increases from 150 to 1,500 A. On other substrata, the behaviour of the coercivity during deposition may be markedly different from the above. If the glass is coated with aluminium a few hundred angstroms thick, for example, which is then oxidized, an initial coercivity of 10–20 oersteds, steadily decreasing during deposition to a value of 1–5 oersteds at a thickness of about 1,500 A. has been found. This behaviour is more like that observed by Tiller and Clark.

The apparatus has also been used to monitor a small number of films electroplated on to a copper base. In these experiments a behaviour similar to that described for the evaporation on to aluminium oxide was obtained.

The use of an alternating aligning field which has a zero value twice in each cycle is perhaps questionable. As, for a similar set of conditions, nearly all specimens exhibit a distinct pattern of magnetic behaviour during deposition, it seems rather unlikely that the variations observed can be attributed to the use of an alternating field. Certainly it is possible to produce magnetic specimens with a well-defined magnetic axis and a relaxation time of less than 200 millimicroseconds in an applied field of twice the coercive field.

These experiments show that the variation of the coercivity of thin films during formation is not a simple relation as given by Néel[1] but is influenced very strongly by secondary effects such as the nature of the substratum.

An apparatus similar to that described above has also been developed by K. E. Drangeid.

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Examination of Particulate Matter on Filter Membranes

Fine filter membranes with maximum pore sizes less than 1μ are now readily available for collecting solid material suspended in a liquid. As the membranes are of very uniform thickness, they may be examined under a microscope for the determination of the sizes and nature of the particles deposited on them. We have used a simple and effective technique for preparing slides incorporating the sample membrane. The essential feature of the method is that the membrane is made transparent to permit the use of transmitted light without disturbing the particle distribution.

A water ejector pump is usually used to assist filtration. By keeping this running the membrane may be dried in a few minutes. With the suction still applied, a fixative is poured down the side of the filter funnel so as to spread steadily across the membrane and be drawn through it. The forces acting on the particles are such that these are held against the membrane and are not disturbed by the advancing liquid front. The fixing process is complete when the fixative has been drawn through the membrane and the latter is again dry.

With the correct choice of fixative the membrane retains its porosity, and is thus capable of being rendered transparent by saturation in Canada balsam diluted with xylene. It can be mounted as desired without fear of disturbing the particles. We have used a solution of 0·5 per cent (w) 'Perspex' in chloroform as the fixative, and found it to be eminently suited to our application.

Where an automatic particle counter is used care must be taken to choose a membrane exhibiting negligible grain when treated, and to ensure that the drying processes are carried to completion, otherwise blotches caused by trapped air or liquid other than balsam may result in counting-errors.

We wish to thank the Directors of 'Shell' Research, Ltd., for permission to publish this communication.

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Refractivity and Lattice Constant Ratios of Lithium-6- and Lithium-7-rich Fluorides

The Industrial Group of the United Kingdom Atomic Energy Authority has provided small quantities of lithium compounds, containing different proportions of the isotopes lithium-6 and lithium-7, for use by its Research and Development Laboratories at Capenhurst.

Some of the material has been converted to lithium fluoride, and the refractivity of vacuum-grown crystals containing respectively (*A*) 90 per cent lithium-6, and (*B*) 95 per cent lithium-7, has been determined in the Natural Philosophy Department, Aberdeen, using a Hilger–Watts 'Research' pattern spectrometer, with 6·5 in. diameter glass circle. Prism *A* has faces 22 mm. × 26 mm., and prism *B*, 35 mm. × 26 mm. The observations were reduced to a uniform temperature of 21° C., and to standard atmospheric pressure.

Table 1. Variation of Refractive Index of Lithium Fluoride with Wave-length

λ (A.)	$n(A)$ (90 per cent lithium-6 fluoride)	$n(B)$ (95 per cent lithium-7 fluoride)	$n(N)$ (normal lithium fluoride).
4471·48	$1{\cdot}39618_{4(6)}$	$1{\cdot}39631_{2(4)}$	1·396310
5015·68	$1{\cdot}39414_{8(7)}$	$1{\cdot}39428_{6(4)}$	1·394289
5893·7	$1{\cdot}39189_{8(6)}$	$1{\cdot}39206_{2(7)}$	1·392066
6678·15	$1{\cdot}39049_{7(2)}$	$1{\cdot}39068_{5(3)}$	1·390683

Table 1 gives indices for four wave-lengths. Each value is the mean of three independent mean values, obtained from measurements on all three angles of the prism. The bracketed figures are the average residual errors ($\times 10^6$). The overall error was 5×10^{-6} for prism *A* and 4×10^{-6} for prism *B*. The last column, with values for the refractive index of normal lithium fluoride, is from measurements by Tilton and Plyler at the National Bureau of Standards[1].

Table 2. Variation with Wave-length of Refractive Index Differences

λ (A.)	$n(B) - n(A)$	$n(N) - n(A)$	$n(B) - n(N)$
4471·48	$12{\cdot}8 \times 10^{-5}$	$+ 12{\cdot}6 \times 10^{-5}$	$+ 0{\cdot}2 \times 10^{-5}$
5015·68	13·8	+ 14·1	− 0·3
5893·7	16·4	+ 16·8	− 0·4
6678·15	18·8	+ 18·6	+ 0·2

Table 2 shows the difference in refractivity between the enriched specimens *A* and *B*, and also between these and normal lithium fluoride. The major variation of 85 per cent in the proportion of lithium-7 from *A* to *B* produces an effect which varies from 13 to 19 $\times 10^{-5}$ in the range considered. Hence the difference of 2·4 per cent between *B* and normal lithium fluoride (92·6 lithium-7) should produce a shift of $n(B) - n(N)$ only ranging from 0·36 to $0{\cdot}53 \times 10^{-5}$ which is of the same order as the error. Moreover, Tilton and Plyler[1] found that there are small variations in the fifth decimal place between prisms of normal lithium fluoride, so that the close agreement shown in the last column between $n(B)$ and $n(N)$ is satisfactory.

The difference in refractivity increases with wave-length and can be fitted closely to an expression $x + y\lambda^2$. Using the least squares method, the values for $n(B) - n(A)$ are $x = 7{\cdot}723$, $y = 24{\cdot}83$ and for $n(B) - n(N)$, $x = 7{\cdot}870$, $y = 24{\cdot}60$. It is suggested that the term x arises primarily from the change in lattice constant, and the variable term from the change in infra-red dispersion frequency with the isotopic fraction.

X-ray measurements by Thewlis[2] show that the lattice constant of lithium-6 fluoride exceeds that of lithium-7 fluoride by 2×10^{-4} parts. This dilation would produce a reduction in refractivity of the order of 20×10^{-5}, were it not partially offset by a rise in the sum of the ionic polarizabilities. However, the net effect of expansion at constant composition is effectively displayed by the temperature coefficient (dn/dT) of normal lithium fluoride, which is $-1{\cdot}65 \times 10^{-5}$ at a mean wave-length in the visible region.

The linear expansion coefficient of lithium fluoride at 20° C. is $3{\cdot}44 \times 10^{-5}$ per deg. C., so that a temperature rise ΔT of about 5 deg. C. produces the same dilation of the lattice in normal lithium fluoride as the change in composition from B to A at constant temperature. The product of the equivalent temperature rise and the temperature coefficient (dn/dT) gives a term of the order of -8×10^{-5}, which is close to the observed values of x. Conversely, x may be used to estimate the lattice dilation, and Table 3 shows the equivalent temperature rise ΔT, the expansion ratio (da/a), the change Δf in the isotopic fraction, and the expansion ratio $(da/a)_{100}$ scaled linearly to a 100 per cent change in isotopic fraction. The mean value is $1{\cdot}94 \times 10^{-4}$, in close agreement with the X-ray value (2×10^{-4}).

Table 3. DATA FOR DERIVATION OF $(da/a)_{100}$

Data	x	ΔT	(da/a)	Δf (per cent)	$(da/a)_{100}$
$n(B)-n(A)$	7·723	4·77	$1{\cdot}64 \times 10^{-4}$	85	$1{\cdot}99 \times 10^{-4}$
$n(B)-n(N)$	7·870	4·68	$1{\cdot}61 \times 10^{-4}$	82·6	$1{\cdot}90 \times 10^{-4}$

The equivalent rise of temperature simulates the effect of an increased amount of lithium-6 at sufficiently high frequencies, but in the visible region there will be a further difference arising from the increase in infra-red dispersion frequency. The refractivity at 23·6° C. of normal lithium fluoride, from 0·4 to 5·9μ, has been represented[1] by a Ketteler–Helmholtz dispersion formula:

$$n^2 = 1 - \frac{5{\cdot}1281966\lambda^2}{797{\cdot}8925296 - \lambda^2} + \frac{0{\cdot}92556295\lambda^2}{\lambda^2 - 0{\cdot}0053160}$$

The second term is of the form $-\dfrac{a\lambda^2}{\lambda^2_R - \lambda^2}$, where λ_R is the effective infra-red dispersion wave-length. Thus a change $d\lambda_R$ with variation in composition will produce a change in refractive index:

$$dn \simeq \frac{a\lambda^2}{n\lambda^2_R}\left(\frac{d\lambda_R}{\lambda_R}\right)$$

which is of the required form $y_c\lambda^2$. Infra-red transmission and reflectivity measurements on materials A and B accord with the assumption that the product $m\lambda_R^{-2}$ is constant[3], where m is the reduced mass, so that the ratio $(d\lambda_R/\lambda_R) = 0{\cdot}0485$ for B and N, giving a calculated value $y_c = 22{\cdot}4$, in substantial agreement with the observed value $y = 24{\cdot}6$. For the B and A observations, the corresponding values are $y_c = 23{\cdot}1$ and $y = 24{\cdot}8$.

Thus the differences in refractivity are in close agreement with those predicted from existing X-ray, dispersion and expansion observations. Fig. 1 shows the variation of $n(B) - n(A)$ with wave-length; the full curve gives the computed values for a dilation $(da/a)_{100} = 2 \times 10^{-4}$, and for a ratio $(d\lambda_R/\lambda_R) = 1{\cdot}05$ appropriate to an 85 per cent change in composition. The residuals are less than $0{\cdot}4 \times 10^{-5}$.

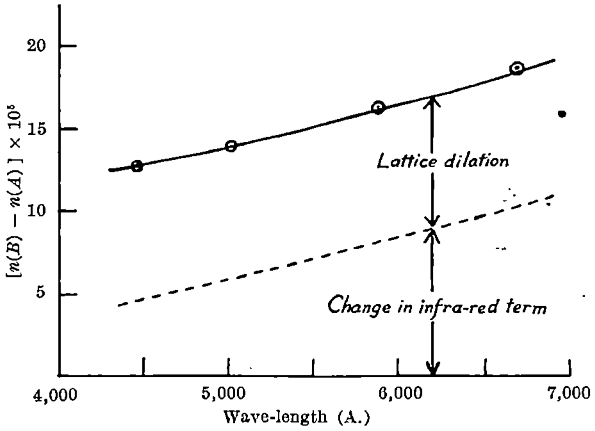

Fig. 1. Excess refractive index of lithium-7 fluoride-rich (B) over lithium-6 fluoride-rich (A) prism. The full curve is the theoretical excess for the observed lattice constant ratio $a(^6\text{LiF})/a(^7\text{LiF}) = 1{\cdot}0002$ and for the increase of 5 per cent in the infra-red dispersion frequency from B to A. The dashed curve is the change arising from the infra-red term alone

We thank the Ministry of Supply for a grant providing the crystal-growing facilities in the Natural Philosophy Department at Aberdeen, and the Chemical Services Department, Capenhurst Works, United Kingdom Atomic Energy Authority, for preparing and analysing the lithium fluoride.

We thank Mr. W. Mitchell for assistance in operating the furnace, and in preparation of the prism blanks, which were polished by Messrs. Barr and Stroud, Ltd., Glasgow.

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Spacing Anomaly in Electron Microscope Images of Crystal Lattices

SINCE Menter's observation[1] on electron microscope images of crystal lattices of metal phthalocyanines, several authors[2-7] have observed a variety of lattices in this way. Interpreting the image in terms of the kinematic theory of electron diffraction and Abbe's theory of image formation, Menter concluded that it should consist of parallel lines with equal spacing. He measured[3] the spacings of many images of platinum phthalocyanine and concluded that their average value does in fact coincide with the spacing of the lattice planes. Uyeda *et al.*[8] suggested that an image of the superlattice spacing of about 90 A. observed in antigorite crystals is useful for checking the magnification of electron micrographs because of its constancy.

In analysing some moiré patterns[9] one of us (H. H.) found local spacing anomalies in the image, where the Bragg reflecting condition was not exactly satisfied.

Similar spacing anomalies have been detected in micrographs of crystal lattices of copper phthalocyanine, platinum phthalocyanine, zinc phthalocyanine and antigorite. A typical anomaly in an electron micrograph of copper phthalocyanine is shown in Fig. 1. The micrograph was cut into two parts perpendicular to the parallel lines of the image and the two parts have been juxtaposed to demonstrate the spacing anomaly clearly. The lines indicated by the arrows coincide with each other on both parts of the photograph ; but there are small relative displacements of the lines in between. The spacing of the weak lines is larger than that of the strong ones, and at the maximum the relative displacement is almost a quarter of the spacing. This type of spacing anomaly has been observed in other crystals associated with regions of different intensity in the line pattern and was found to move with the movement of the region of different intensity.

The anomaly may be explained by the dynamical theory of electron diffraction. When the angular setting of the crystal deviates slightly from the Bragg position, the wave vectors of the primary and reflected waves in the crystal change from those at the Bragg setting. Since the image is formed by the interference of primary and reflected waves, it may be expected that the image will vary with the deviation from the Bragg angle. Some calculations, reported in detail elsewhere, have been made on this basis where one Bragg reflexion only is excited, and these explain the anomaly satisfactorily.

The calculation shows that the lattice image of a plate-shaped crystal is composed of parallel lines, but the positions of the lines do not necessarily coincide with the positions of the potential maxima in the crystal, and, moreover, the contrast of the image changes both with the thickness of the crystal and the deviation from the Bragg angle. In a bent plate-shaped crystal the lattice image is formed only on the extinction contour. In the centre of the contour where the Bragg condition is satisfied exactly the spacing of the image is equal to that of the original lattice, but it deviates from this either by expansion or contraction near the edge where the Bragg condition is not exactly satisfied.

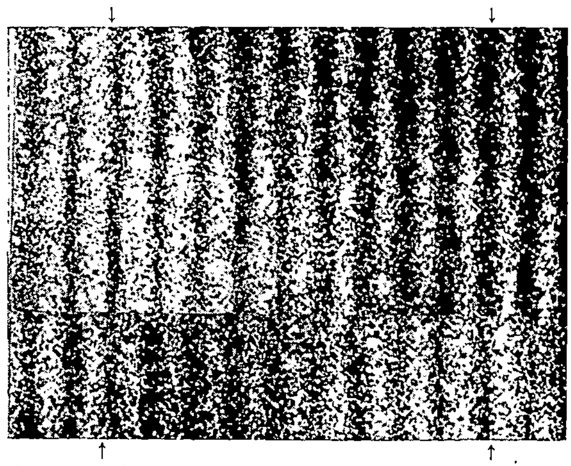

Fig. 1. Electron micrograph of crystal lattice of copper phthalocyanine with spacing anomaly. This can easily be detected by comparing the upper part with the lower part of the micrograph ; the micrograph has been divided into two parts by cutting across the image. The arrows indicate the positions where the corresponding lines coincide with each other on both parts of the micrograph

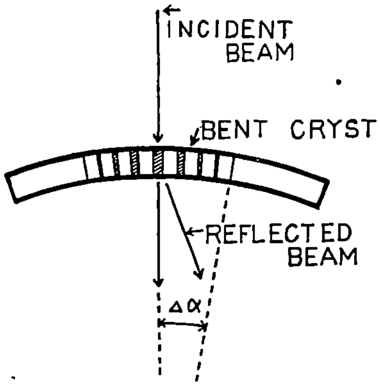

Fig. 2. Relation between the incident beam and uniformly bent crystal. Δα is an angle of bending

For example, if a crystal is bent into the form of a cylinder as shown in Fig. 2 and the thickness of the crystal is $t_0 = \lambda E/4V_g$ (where λ is wave-length, E is accelerating potential, V_g is the Fourier coefficient of the crystal potential, which is about 240 A. and 300 A. for the $20\bar{1}$ plane of copper phthalocyanine and platinum phthalocyanine respectively), the image in the centre of the extinction contour has the true spacing of the crystal lattice and maximum contrast, whereas near the edge of the contour the spacing is increased and the contrast lowered. If the thickness is $2t_0$ the image does not appear along the centre of the extinction contour but only at the brim with increased spacing. If the thickness is $3t_0$ the contrast of the image at the centre is reversed compared with that at t_0, that is, the positions of the lines shift by one-half spacing.

The thickness and mode of bending of the crystal shown in Fig. 1 are not known exactly, but it is estimated that the former is several hundred angstroms and the local bending can easily be larger than that corresponding to the angle $\Delta\alpha = 8 \times 10^{-3}$ rad. necessary to shift the image by one-quarter spacing. The calculation given above is therefore probably applicable to the present observation. It should be noted that the spacing anomaly may occur sometimes both as a result of bending and as a result of thickness variation across the crystal. It is concluded that the anomaly is not due to any anomaly in the crystal lattice spacing but arises from the dynamical effects in scattering of electrons by crystals.

We wish to express our sincere thanks to Prof. K. Tanaka and Prof. R. Uyeda for useful discussions.

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Feb. 12.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, April 6

British Institution of Radio Engineers, Computer Group (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 3 p.m. and 6 p.m.—Symposium on "Large Capacity Storage Devices".

Institution of Electrical Engineers (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "Co-operation between the Electricity and Gas Industries" opened by Mr. F. C. Smith, M.B.E.

Society of Engineers (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. George Constantinesco: "Sonics".

Society of Chemical Industry, London Section (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Mr. W. A. M. Edwards: "Chemical Industry and the Free Trade Area".

Radar and Electronics Association (at the Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2), at 7 p.m.—Dr. T. E. Allibone, F.R.S.: "Thermonuclear Research".

Monday, April 6—Wednesday, April 8

Society for General Microbiology (in the Beveridge Hall, Senate House, University of London, W.C.1)—Twenty-eighth General Meeting.

Monday, April 6—Friday, April 10

Fifth International Instrument Show (at 4 Tilney Street, Park Lane, London, W.1).

Tuesday, April 7

Physical Society, Acoustics Group (joint meeting with the Institute of Physics, in the Physics Department, The University, Southampton)—All-day Symposium on "New Techniques in the Analysis of Noise and Vibration".

Institution of Electrical Engineers, Measurement and Control Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. M. E. Haine and Mr. J. Vine: "An Electron Trajectory Tracer for use with the Resistance Network Analogue".

Society of Chemical Industry, Plastics and Polymer Group (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Dr. J. Haslam and Mr. A. R. Jeffs: "Applications of Gas-Liquid Chromatography to the Work of a Plastics Analytical Department"; Mr. C. D. D'Oyly-Watkins, Mr. G. L. Palmer and Mr. C. M. Robertson: "Differential Thermal Analysis of some High Polymers".

Tuesday, April 7—Friday, April 17

Factory Equipment Exhibition (at Earls Court, London, S.W.5).*

Wednesday, April 8

Chemical Society (in the Large Hall, Friends House, Euston Road, London, N.W.1), at 10.30 a.m.—Prof. H. J. Emeléus, F.R.S.: "Some Inorganic Polymers" (Presidential Address).

Geological Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. L. Berry and Mr. B. P. Ruxton: "The Structure and Form of Hong Kong Harbour"; Dr. W. S. Pitcher and Prof. H. H. Read: "The Aureole of the Main Donegal Granite".

Institution of Mechanical Engineers, Internal Combustion Engine Group (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "What is the Present Position of the Gas Turbine Relative to the Diesel Engine for Satisfactory Stationery, Marine and Automobile Applications".

Physical Society (in the Main Lecture Theatre, The Physiology Laboratory, The University, Oxford), at 8.30 p.m.—Prof. H. S. W. Massey, F.R.S.: "Collisions" (43rd Guthrie Lecture).*

Thursday, April 9

Royal Anthropological Institute (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Dr. Raymond Allchin: "The First Settlers in South India: Recent Research at Neolithic Sites in the Deccan".

Institute of Biology, London Branch (joint meeting with the Chelsea College of Science and Technology Biological and Geological Societies, at the Chelsea College of Science and Technology, Manresa Road, London, S.W.3), at 7 p.m.—Meeting on "Modern Ideas of Continental Drift". Speakers: Dr. J. A. Clegg and Dr. A. J. Cain.

Friday, April 10

Royal Astronomical Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Prof. A. A. Mikhailov: "The Deflection of Light by the Sun's Gravitational Field" (George Darwin Memorial Lecture).

Medical Research Council (at the National Institute for Medical Research, Mill Hill, London, N.W.7), at 5 p.m.—Dr. S. E. Luria (Massachusetts Institute of Technology, Cambridge, Mass.): "Mechanisms of Infective Heredity in Bacteria".*

Institution of Mechanical Engineers (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Dr. W. B. Lewis: "Canadian Atomic Energy Development in Review and Prospect" (James Clayton Lecture).

Radar and Electronics Association (at Norwood Technical College, Knight's Hill, London, S.E.27), at 7 p.m.—Mr. D. C. Thomas: "A Modern British Marine Radar" (The B.T.H.601 "Escort").

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Assistant Psychologist (with an honours degree or equivalent qualification in psychology, and preferably postgraduate research experience in experimental or clinical psychology)—The Secretary, The National Hospital for Nervous Diseases, Queen Square, London, W.C.1 (April 10).

Plant Breeder (with an honours degree in botany and experience in plant breeding or a postgraduate qualification in genetics or plant breeding) in the Tea Research Institute of Ceylon—Dr. F. R. Tubbs, East Malling Research Station, near Maidstone, Kent (April 10).

Assistant Lecturer or Lecturer in Applied Mathematics—The Secretary, The University, Exeter (April 11).

Assistant Physicist (with an honours degree in physics and preferably some previous experience of hospital physics) in the Radiotherapeutic Centre, for duties concerned with a wide variety of applications of physics to clinical radiotherapy and other branches of medicine—The Secretary, Addenbrooke's Hospital, Cambridge (April 11).

Lecturer (with a special interest in stratigraphy) in Geology—The Secretary, The University, Edinburgh (April 11).

Lecturer (preferably with an interest in molecular weight measurement or nuclear magnetic resonance) in Physical Chemistry—The Secretary, The University, Aberdeen (April 15).

Lecturer (with a special knowledge of the strength of materials, or theory of machines, or applied thermodynamics) in Mechanical Engineering; and a Lecturer (with a special knowledge of applied aerodynamics and/or aircraft performance) in Aeronautical Engineering—The Principal, Coventry Technical College, Butts, Coventry (April 16).

Senior Lecturers, Lecturers, and Assistant Lecturers (honours graduates, preferably with research experience) in the Department of Physics—The Clerk to the Governors, Chelsea College of Science and Technology, Manresa Road, London, S.W.3 (April 18).

Assistant Lecturer in Physics—The Registrar, University College of North Staffordshire, Keele, Staffs (April 20).

Lecturer in Archæology—The Secretary, The Queen's University, Belfast (April 20).

Superintendent of Laboratories in the Department of Chemistry—The Registrar, University College, Singleton Park, Swansea (April 20).

Fellow (honours graduate in some branch of chemistry, with some postgraduate research experience) in Protein Chemistry in the Division of Protein Chemistry, C.S.I.R.O., Parkville (near the University of Melbourne), to apply ultra-violet and visible spectrophotometry in studies of the chemistry of extracted wool proteins and related model compounds and to relate the findings to similar measurements on the intact fibre—The Chief Scientific Liaison Officer, Australian Scientific Liaison Office, Africa House, Kingsway, London, W.C.2, quoting Appointment No. 463/116 (April 25).

Lecturer in Inorganic Chemistry—The Registrar, University College of Wales, Aberystwyth (April 25).

Lecturer in the Department of Mathematics, University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa, April 25).

Lecturer (with qualifications in either chemistry or physics or glass technology) in the Department of Glass Technology—The Registrar, The University, Sheffield (April 25).

Lecturer (with special qualifications in fluid dynamics) in Mathematics—The Secretary of Faculties, University Registry, Oxford (April 25).

Lecturer in Philosophy—The Secretary, Balliol College, Oxford (April 30).

Research Fellow (with a Ph.D. degree or equivalent research experience in physical-organic chemistry or biochemistry) in the Chemistry Department, for an investigation of the mode of action of germicides—The Professor of Chemistry, The University, Hull (April 30).

Scientific Officer (with a good honours degree, preferably with postgraduate experience) in the Plant Pathology Department, to work on virus diseases of field crops—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (April 30).

Assistant Lecturer (interested in plant physiology or the genetics of micro-organisms) in Botany; and an Assistant Lecturer in Psychology—The Registrar, The University, Hull (May 1).

Director of the Institute of Statistics—The Registrar, University Registry, Oxford (May 2).

Lecturer (with good academic qualifications and experience in one of the following fields: electrical power engineering, electrical engineering materials, or electrical engineering physics) in the Department of Electrical Engineering—The Registrar, The University, Leeds 2 (May 2).

Reader in Mechanical Engineering at Imperial College—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 6).

Lecturer in Pure Mathematics—The Secretary, The Queen's University, Belfast (May 8).

Chair of Physics—The Registrar, University College of North Staffordshire, Keele, Staffs (May 9).

University Students or Fellows, for experimental or theoretical research in nuclear and elementary particle physics—The Professor of Natural Philosophy, The University, Glasgow, W.2 (May 9).

Chair of Education at University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (May 10).

Lecturer in Physics; and Lecturers (2) in Anatomy—Joint Clerk to the University Court, Queen's College (University of St. Andrews), Dundee (May 16).

Lecturer (preferably with an interest in histology and biochemistry) in Physiology—The Secretary of University Court, The University, Glasgow (May 16).

Assistants (either sex, with a good reading knowledge of Russian or Italian, and preferably with scientific interests), for abstracting papers in economic entomology—The Director, Commonwealth Institute of Entomology, 56 Queen's Gate, London, S.W.7.

Chief Plant Protection Officer (with a degree in entomology and considerable experience in economic entomology and plant quarantine services) in the Ministry of Agriculture and Lands, Jamaica, to direct and supervise the Plant Protection Division (including Entomology and Plant Pathology Sections), and to maintain an effective plant quarantine service—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/32/023.

Laboratory Technologist (Plant Pathologist) (with a university degree with botany as the main subject) in the Department of Agriculture, Kenya, to assist with laboratory research and field experiments in problems of coffee pathology and physiology—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/7/046.

Lecturer (with research and teaching experience) in Plant Physiology—The Professor of Plant Physiology, Imperial College of Science and Technology, Prince Consort Road, London, S.W.7.

Master (graduate) to teach Mathematics, Pure and Applied, up to Advanced Level—The Director of Studies, The Nautical College, Pangbourne, Berkshire.

Reader (with a good degree of a British university, research qualifications in some branch of applied mathematics or statistics, and preferably experience of teaching in a university or major technical college) in Applied Mathematics—The Clerk to the Governing Body, Battersea College of Technology, London, S.W.11.

Readers, Senior Lecturers and Lecturers in Chemistry, Electrical Engineering, Civil Engineering, Mechanical Engineering and Physics; and Senior Lecturers and Lecturers in Chemical Engineering, Metallurgy, Pharmaceutical Chemistry, Pharmaceutics, Pharmacology, Mathematics, Statistics and Zoology—The Registrar, Bradford Institute of Technology, Bradford 7.

Soil Surveyor (with a university degree, preferably with honours, in agricultural chemistry or pure chemistry, or, alternatively a degree in geology or geography, and a good knowledge of chemistry) in British Guiana, for soil surveys on the coastlands and the underdeveloped interior—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/30/017.

REPORTS and other PUBLICATIONS

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Great Britain and Ireland

Government of Northern Ireland: Ministry of Agriculture. Leaflet No. 13: Contagious Abortion and Infectious Sterility of Cattle. Pp. 8. (Belfast: Ministry of Agriculture, 1958.) [102

Northampton College of Advanced Technology. Prizes and Certificates, Session 1957–1958. Pp. 26. (London: Northampton College of Advanced Technology, 1959.) [102

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On Being a Technologist. By Prof. D. G. Christopherson. (Technics and Purpose, No. 5.) Pp. 33. 2*s*. 6*d*. net. The Educated Man Today and Tomorrow. By Sir John Wolfenden. (Technics and Purpose, No. 6.) Pp. 25. 2*s*. 6*d*. net. (London: SCM Press, Ltd., 1959.) [102

Ministry of Labour and National Service. Studies in Official Statistics No. 4: The Length of Working Life of Males in Great Britain. Pp. 24. (London: H.M. Stationery Office, 1959.) 3*s*. 6*d*. net. [102

The Civic Trust. Your Town: an Outline of the Work of an Amenity Society. Pp. 20. 1*s*. The Civic Trust. (A paper on the first year's work presented by Sir Howard Robertson, a Trustee of the Civic Trust, to the 58th National Conference of the National Housing and Town Planning Council, Brighton, 22nd October, 1958.) Pp. 7. (London: The Civic Trust, 79 Buckingham Palace Road, 1959.) [112

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Other Countries

United States Department of the Interior: Geological Survey. Bulletin 1000-H: Geochemical Prospecting Studies in the Bullwhacker Mine Area, Eureka District, Nevada. By Alfred T. Miesch and Thomas B. Nolan. Pp. iii+397–408. 15 cents. Bulletin 1042-F: Geology and Coal Resources of the Tiptop Quadrangle, Kentucky. By Stewart W. Welch. Pp. iv+585–612+plates 50–55. n.p. Bulletin 1042-R: Geology of the Ord Mine, Mazatzal Mountains, Quicksilver District, Arizona. By John N. Faick. Pp. iii+685–698+plates 58–60. 1 dollar. Bulletin 1046–J: Geologic Features of Areas of Abnormal Radioactivity South of Ocala, Marion County, Florida. By Gilbert H. Espenshade. Pp. iii+205–219+plates 12–15. 1 dollar. Bulletin 1053: Geology and Coal Resources of the Centralia-Chehalis District, Washington. By Parke D. Snavely, Jr., R. D. Brown, Jr., and Albert E. Roberts. With a Section on Microscopical Character of Centralia–Chehalis Coal by J. M. Schopf. Pp. vi+159+13 plates. n.p. Bulletin 1059–F: Selected Annotated Bibliography of the Geology and Occurrence of Uranium-Bearing Marine Black Shales in the United States. By Carolyn E. Fix. Pp. iii+263–325+plate 3. 25 cents. Bulletin 1061-D: Quaternary Geology of Boulder Mountain, Aquarius Plateau, Utah. By Richard F. Flint and Charles S. Denny. Pp. iv+103–164+plates 6–8. 1 dollar. Bulletin 1070-B: Lead-Alpha Ages of the Mesozoic Batholiths of Western North America. By Esper S. Larsen, Jr., David Gottfried, Howard W. Jaffe and Claude L. Waring. Pp. iv+35–62. 15 cents. (Washington, D.C.: Government Printing Office, 1958.) [281

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Peabody Museum of Natural History, Yale University. Bulletin 12: Natural History of the Marine Sponges of Southern New England. By Willard D. Hartman. Pp. xi+155+11 plates. Bulletin 13: Notes on a Collection of Birds from Mindoro Island, Philippines. By S. Dillon Ripley and D. S. Rabor. Pp. iv+82. (New Haven, Conn.: Peabody Museum of Natural History, Yale University, 1958.) [102

International Geophysical Year. Second Report of the Makerere College Ruwenzori Expedition, June 1958. Pp. 30. (Kampala: Geography Department, Makerere College, 1958.) [102

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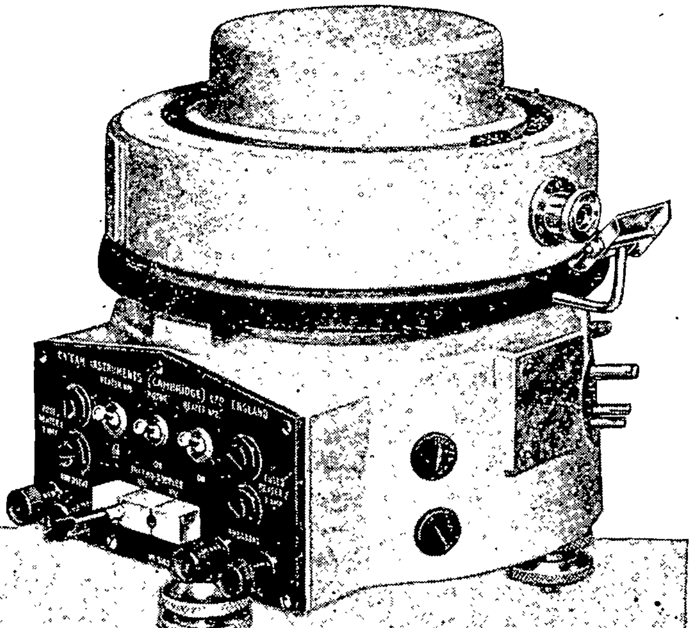

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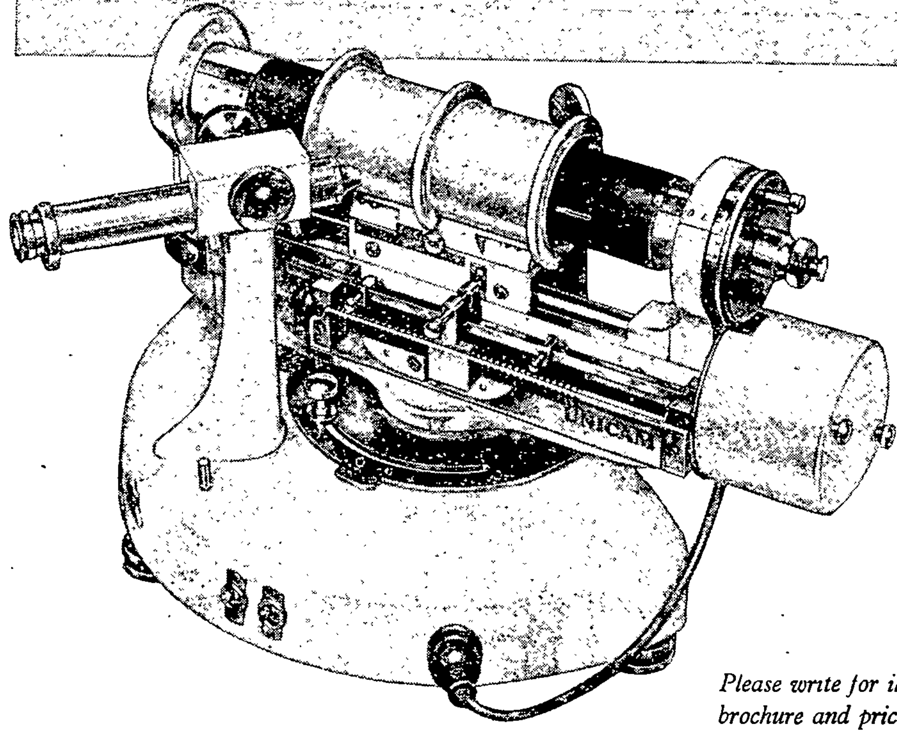

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EXPANSION OF MARINE RESEARCH IN THE UNITED STATES

THE National Academy of Sciences – National Research Council has issued a statement making known the conclusions of a Committee which was set up at the request of a number of Government agencies to review the progress and needs of marine science in the United States. The full report is promised in the near future. The main conclusions are encouraging because they show that many of the problems that have long been too large and perplexing to attract close attention are becoming more approachable and promising; they are also disturbing because they show that progress, though commendable, does not match growing needs for detailed information and understanding of the oceans.

The statement mentions the need for increased food supplies. The main factor leading to high fertility in the oceans is active mixing and upwelling from the deep layers, where nutrients are regenerated, to the illuminated surface layer where the plants grow. Upwelling is not confined to coastal regions, or to oceanic islands and shoals, and it can occur wherever there are sharp differences and changes in the surface and sub-surface currents. Such areas, far from land, are already forming the basis of ocean fisheries, and the factory ships that will fish them will need good understanding of the fundamental physics and biology as well as the breeding, feeding and migratory habits of the fish to ensure economical working with regular catches.

The need for more understanding of fluctuations and trends in climate is also emphasized. The heat capacity of the oceans is very much larger than that of the atmosphere, and the oceans are largely responsible for the thermostatic control that makes so much of the Earth habitable. They gather the Sun's heat and distribute it as moisture-laden air in a pattern determined by complex interaction between sea and air, currents and winds. The slow but powerful changes in the oceans have important effects on agriculture, fisheries, ice conditions and sea-level. All the great hurricanes and typhoons start over the sea.

Modern studies of waves, tides, currents and movements of sediments have much to offer to ship designers, coastal and harbour engineers, and to those concerned with special aspects of navigation, salvage and oil drilling. The National Academy Committee, however, gives special emphasis to the needs of military defence. With every fresh advance in surface, amphibious and undersea warfare, the side with the fullest knowledge and most detailed understanding of the oceans is likely to gain some advantage in devising new techniques, discarding out-of-date ones and judging how to proceed. The report mentions the submarine menace and maintains that "from the point of view of military operations there is no comparison between the urgencies of the problems of the oceans and those of outer space". Concern that the new fascination of space will divert American scientists and the Government from the vast unexplored regions and problems of the oceans is implied throughout the statement.

The study of the sea floor has made tremendous strides during the past five years. With the help of new tuning-fork controlled echo-sounders the floor of the deep ocean can be charted in nearly as much detail as a river estuary, and the half-inch to a mile maps, photographs, cores and dredges reveal fascinating new information about active movements of water and sediment, eroded channels, possible mineral resources and the habits of bottom-living animals. The time has come when geology can be actively extended to the rocks and sediments at the bottom of the oceans.

The main recommendations of the Committee are that basic research in marine science should be doubled within the next ten years, and that the research effort should be supplemented by ocean-wide surveys. The resources of the present surveying effort, mainly that of the U.S. Coast and Geodetic Survey, would be doubled for the purpose. The whole programme would be strengthened by expanded application of the science to military defence, marine resources and the problems raised by the use of nuclear energy.

The first step towards the Committee's objective is the provision of new ships with the character of floating laboratories, and others for survey. The need for new devices such as submarines, mid-ocean platforms and unmanned buoys is emphasized, and new instruments and telemetering equipment are needed. It is estimated that each ship needs sixty hore-based scientists and technicians, and the difficulty of attracting men with the essential skill and enthusiasm is clearly recognized as the greatest difficulty.

Oceanography is no longer a descriptive subject; some of its theoretical and practical work is as advanced, as difficult and as likely to find useful applications in other sciences, as that done in any research laboratory. The subject has begun to attract attention in universities, especially in the United States, and the Committee feels that its difficulties may be surmounted by more deliberate measures to encourage interchange with universities. There can be no subject of wider and more rapidly growing interest or of more potential world value, and yet there is a shortage of qualified postgraduate research workers because the specialized facilities that might be used to continue university training are not used to the full, and the universities have few of their own. This problem will become more acute as the work in progress outside the universities requires increasing numbers of workers with more and more specialized qualifications; to solve it the Committee advocates affiliation of oceanographic research institutions with university faculties, and the development of new centres at universities.

The Committee proposes a ten-year plan costing 651 million dollars over and above the present level of expenditure. The plan is described as 'minimal' to meet long-range requirements, and it is stated that action on a scale appreciably less "will jeopardize the position of oceanography in the United States relative to the position of the science in other major nations, thereby accentuating serious military and political dangers, and placing the nation at a disadvantage in the future use of the resources of the sea".

The report has no official Government approval, but opinion in the United States expects it to guide the course of national support for marine science. Oceanographic research has already been earmarked by the President's Science Advisory Committee as one of the major scientific fields needing more emphasis. Further afield it is also of interest. From its very nature, oceanography is dependent on, and contributes to, most of the other sciences; moreover, its pursuit involves international collaboration on an extensive scale. Any increased support in the United States for oceanography will contribute to the development of the science and set an example which other countries might well follow.

EARLY AMERICAN NATURALISTS

John and William Bartram's America

Selections from the Writing of the Philadelphia Naturalists. Edited with an Introduction by Helen Gere Cruickshank. Pp. xxii+418. (New York: The Devin-Adair Company, 1957.) 5 dollars.

The Travels of William Bartram

Edited with commentary and an annotated index by Francis Harper. Naturalist's edition. Pp. lxi+727+42 illustrations and facsimiles. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1958.) 68*s*. net.

THE Quakers John Bartram and his son William were two of America's leading naturalists throughout the eighteenth century—their combined lives cover a span of nearly one hundred and twenty-five years, from 1699 until 1823. Although they were primarily botanists, and John established the first botanic garden in America near Philadelphia about 1730, they were widely interested in all aspects of natural history. In their early days there were few books that could help them in classifying the numerous undescribed species that they found, but when a merchant friend in Philadelphia took some of John's collections and observations to Peter Collinson of London, who immediately appreciated their value, a correspondence was started that lasted nearly fifty years. As a result of John's friendship with Collinson he entered into correspondence with nearly all the naturalists of Europe, including Linnæus and Sir Hans Sloane, and was elected into the fellowship of the Royal Society, and appointed "Botanist to His Majesty for the Floridas".

Both the Bartrams travelled extensively in pursuit of their studies, venturing far beyond the scattered settlements of the outposts into Indian territory where they endured many discomforts and hardships and not a few dangers. In 1743, John accompanied an expedition to make a treaty of peace with the Iroquois and travelled north to Oswego on the shores of Lake Ontario, but his major explorations were made twenty years later in Florida, a region which made a deep impression upon both him and his son. Afterwards, William also spent five years travelling through the Carolinas, Georgia, and Florida, gathering specimens and recording his observations. John was brought up to farming and had very little schooling; although he kept diaries of his travels he did not publish them and they were incorporated into the accounts printed by other members of his expeditions. William Bartram, however, had a fluent pen, and in 1791 he published at Philadelphia his "Travels through North and South Carolina, Georgia, East and West Florida", which was at once reprinted in London and Dublin, and translated into several foreign languages. This book, containing most interesting topographical, anthropological and biological observations, reveals him as a delightful character, full of curiosity, sympathy, and an appreciation of wild Nature rare in those days when the age of elegance regarded everything remote from the centres of civilization as a dreadful wilderness full of savage and horrid prospects.

The first of the volumes under review is an anthology of writings by, and about, the Bartrams, and is an excellent introduction for the general reader to the works of these pioneers. "Although William was one of the foremost of the earliest generation of American writers on natural history and travel, his work has never been known and appreciated in America the way it was abroad." There is no longer any reason for the prophet to be without honour in his own country. The second book is very much more ambitious. It is a reprint of the first edition of William's travels with a long and interesting introduction by Francis Harper, and a valuable commentary identifying the places visited, and the plants and animals seen, based upon extensive journeys made over Bartram's trails and upon much literary research. There is also a copious annotated index, an interesting section of illustrations and a number of maps. William Bartram's narrative is a fascinating account of America nearly two hundred years ago, and Harper's faithful editing enhances its lustre.

L. HARRISON MATTHEWS

RUDIMENTARY GOVERNMENT

Tribes without Rulers

Studies in African Segmentary Systems. Edited by John Middleton and [the late] David Tait. Pp. xi+234. (London: Routledge and Kegan Paul, Ltd., 1958.) 28*s*. net.

SEGMENTARY political systems constitute one of two main types of indigenous political organization found in Africa. Unlike the centralized type, they have no forms of general tribal government vested in chiefs or courts of law or any other overriding authority. They are made up of a collection of mutually independent segments, most commonly based on descent, which maintain law and order among themselves by various forms of self-help, including often the feud, and by making use of kinship, local and ritual bonds. Tribes of this type were, in the 'thirties, frequently recalcitrant to the efforts of colonial governments to devise for them administrative patterns in line with the aims of indirect rule. A handicap here was the paucity of ethnographic information on African political institutions and the consequent inadequacy of theoretical understanding of how they worked.

A beginning was made in the systematic study of the subject when, in 1940, Prof. Evans-Pritchard and I brought out a collection of essays describing a representative series of African political systems ("African Political Systems", edited by M. Fortes and E. E. Evans-Pritchard, 1940). The distinction between the centralized type and the segmentary type was there suggested. Post-war field research has so extended the range and quality of our ethnographic knowledge of Africa that this typology is now seen to be too broad. More thorough analysis of each type is now possible, and the present book makes a welcome beginning with this task. All the contributors belong to the post-war generation of social anthropologists. The six societies they deal with in the book were barely known before the Second World War. Certainly their indigenous political institutions could not then have been analysed with the technical proficiency and theoretical understanding shown by the editors and their fellow contributors.

The peoples described in the present book live in West Africa, the Sudan and East Africa. They vary from sedentary cultivators occupying clearly defined villages, like the Bwamba of Uganda, admirably described by Dr. Winter, to the transhumant cattle-keeping Dinka of the Sudan, whose complex social structure is skilfully elucidated by Dr. Lienhardt, and the widely dispersed, near-anarchic, Konkomba farmers and fighters of Ghana, described with great insight by the late Dr. David Tait, one of the editors. They differ widely in language, custom and belief. What they have in common is a segmentary political-structure based on some form of kinship and descent group.

In addition to the six essays, there is a valuable introduction by the editors. They demonstrate that the segmentary type really includes a range of varieties. They propose a division into three groups, an important distinction being the manner in which the genealogical and local segments are constituted and combined into what they call "jural communities". The analysis of the economic, military, juridical and religious sanctions correlated with this classification is particularly instructive. The book is a significant addition to the growing body of field research on non-western political institutions. It is also, as Prof. Evans-Pritchard remarks in his preface, a fitting memorial to Dr. Tait, who died in a motor accident before it was published. M. FORTES

SOLID STATE PHYSICS

Solid State Physics

By Prof. Adrianus J. Dekker. Pp. xiv+540. (London: Macmillan and Co., Ltd., 1958.) 45*s*. net.

IN recent years various text-books on solid state physics have been published, not without some influence on each other. At first sight, particularly with respect to selection of topics, Prof. Dekker's book bears a likeness to that of Kittel. However, more careful inspection reveals a different appreciation of the various aspects of the subject. There is evidence of the skilled teacher of modern physics with an awareness of the large range of mathematical ability among his student readers. The first nine chapters require little knowledge of the electronic characteristics of solids, beginning with a brief introduction to crystallography and moving all too rapidly through specific heats of solids, lattice defects, dislocation theory, dielectrics, ionic conduction and ferroelectricity. However, the presentation in each case is skilful enough to promote curiosity and wider reading in more specific texts. A further feature is the stressing of fundamentally important matters, for example the emphasis on the Debye theory of specific heats, though with proper indication of the more complex and, practically, almost unwieldly problem of lattice vibration spectra. To mention another chapter, that on ferroelectrics is lucidly written especially in the reference to the thermodynamic theory.

It is natural that the electronic properties of solids find a large place in this book. Non-polar crystals are emphasized, together with their applications in transistors. Complete chapters are devoted to luminescence and secondary electron emission, respectively, while the last part of the book deals with modern magnetism, inclusive of resonance phenomena and their importance in solid state research. If one looks for faults, and these are few, I feel that omission of dielectric breakdown might be remedied in the future and there might also be afforded a little more space for treatment of types of binding in solids.

Each chapter carries a number of exercises or problems; there are an adequate subject index and some useful appendixes. One more favourable comment must be added, about the surprisingly modest price of the volume compared with similar publications and with its equivalent price in the United States. G. F. J. GARLICK

NEW DRUGS USED BY PSYCHIATRISTS

The New Chemotherapy in Mental Illness

The History, Pharmacology and Clinical Experiences with Rauwolfia, Phenothiazine, Azacyclonol, Mephenesin, Hydroxyzine and Benactyzine Preparations. Edited by Dr. Hirsch L. Gordon. Pp. xviii+762. (New York: Philosophical Library, 1958.) 12 dollars.

THIS book is a collection of 119 articles by 167 authors, the majority of whom are American psychiatrists, relating their personal experiences with one or several of the new drugs used in mental illness. The individual writers address themselves to the practising physician and give their impressions, views, recommendations and warnings based either on the material they may have had at their disposal or on their personal philosophical outlook. This leads to statements so contradictory that they become rather disconcerting. Thus one author states on p. 99 that combined therapy with chlorpromazine and reserpine produces a prohibitively high incidence of serious untoward effects, whereas another worker assures us on p. 397 that this combination lacks toxicity and side effects, and he recommends it (p. 400) in neuropsychiatric treatment because of its "advantages over the use of either agent when employed alone". A third group of authors (p. 423) takes the intermediate view that the combination of the two drugs is probably not superior to the use of either drug alone, but that the toxic effects of larger doses are enhanced. That views on therapeutic successes are notoriously apt to be based on faith rather than on fact explains such contradictory opinions; yet methods of clinical trial are available nowadays which overcome these difficulties and yield reliable insight. A few carefully conducted trials, such as that described on p. 13 by H. A. Bowes who was trying to assess the value of azacyclonol ('Frenquel'), are more valuable than any number of uncontrolled clinical impressions. There are many valuable and well-founded observations in the book, but each article has to be scrutinized for the way in which the conclusions were reached before the reader can accept them as valid. The first seventh of the book contains articles of a somewhat more general nature than the later papers which relate clinical experiences only, but even in this section papers based on clinical impressions only are found side-by-side with others of a more objective nature.

If this book is to guide the practitioner through the labyrinth of neuropharmacology, care must be taken over nomenclature. The table on p. xvii is seriously misleading. Thus it suggests that 'Largactil', 'Megaphen' and 'Thorazine' are different compounds because it lists them alphabetically with other phenothiazines without revealing that they are identical. Even more confusing is the placing of 'Meratran' under the heading 'azacyclonol' and of meprobamate under the heading 'mephenesin', as this suggests that, for example, 'mephenesin' could be used as an alternative and more general name for meprobamate.

The main drugs covered by the book are shown in the title; more than 75 per cent of the material deals with reserpine and chlorpromazine.

Marthe Vogt

SOVIET PSYCHOLOGY

Psychology in the Soviet Union

Edited with an Introduction by Brian Simon. Translated by J. and M. Ellis, J. McLeish, H. Milne, N. Parsons and others. (International Library of Sociology and Social Reconstruction.) Pp. viii+305. (London: Routledge and Kegan Paul, Ltd., 1957.) 32*s*. net.

This book derives from the work of the Russian physiologist Pavlov, to whom the Western world accords the respect due to a great scientist. It comprises twenty-two papers contributed by contemporary Soviet psychologists and selected as representative by Prof. A. A. Smirnov and N. A. Menchinskaya of Moscow. Their emphasis is upon human rather than upon animal behaviour, and the studies are frequently in terms of the development of the individual.

The field covered by the nineteen Soviet contributors deals with the principal areas of interest to their Western counterparts. Prof. B. G. Ananiev (Leningrad) deals with problems of perception; Prof. L. V. Zankov (Moscow) with memory, and Prof. E. A. Milerian (Kiev) with attention. The paper on psychopathology by Prof. A. R. Luria (Moscow) suggests close research association of Soviet psychologists with neurophysiologists and psychiatrists. Several papers deal with thinking, apparently a subject of considerable interest to the Russian investigators.

It is on the subject of learning that British and American psychologists have derived most from Pavlov's work: the learning process is now given a central place in the subject-matter of modern experimental psychology. The papers in this field deal with the subject somewhat differently and principally in an educational context, rather than in terms of the more usual technique of the Western psychologist, namely, in the context of animal experiments. Thus, for example, Prof. N. A. Menchinskaya (Moscow) sets out to show how the principles governing learning can be applied to improvement of methods of instruction, and reports experiments on the use of visual techniques in training people to think abstractly in mathematics and elsewhere.

Psychology, presented from the point of view of dialectical materialism, exhibits certain characteristics which merit contrast with Western psychology. The Russian work emerges as heavily experimental; the method of psychometric measurement that is also prominent in British psychology is noticeably absent. Again, some of the contributors, notably Prof. B. M. Teplov (Moscow), reject the idea current in Western psychological theory that principles and laws are not "immutable" and "objective" parts of Nature but simply tools for making predictions about natural phenomena. In their theory the Russian contributors exhibit a distinct preference for theoretical concepts of a physiological kind. Contemporary Western theorists, by contrast, are sharply divided as to whether basic units of analysis should be physiological or of some other kind (for example, logical or mathematical).

A paper by Prof. A. A. Smirnov (Moscow) assesses achievements and omissions of Soviet work in the period 1953–55. Here and elsewhere, one notes the wide range of complex psychological processes to which Pavlovian concepts and techniques have been applied: these applications will certainly interest British and American investigators. Despite the explicit rejection of the method of introspection by Prof. Teplov, Prof. Smirnov makes a plea for more study of—among other things—the complex problem of differences of mental imagery. He also makes reference to the need for more study of the history of world psychology, and for more application of the results of completed researches.

A concluding paper gives a Russian assessment of the Fourteenth (Montreal) International Congress of Psychology and indicates that interaction between Western and Soviet psychology is in progress. This book should stimulate more such interaction. The editor, contributors and translators merit our thanks for this valuable and interesting book.

Peter McKellar

MUSCLE PHYSIOLOGY

Die Muskeltätigkeit

Versuch einer Biophysik des Quergestreiften Muskels. Von Prof. Eugen Ernst. Pp. 355. (Budapest: Verlag der Ungarischen Akademie der Wissenschaften, Akadémiai Kiadó, 1958.) n.p.

In the introduction to his book, Prof. Ernst describes the difficulty that he had in deciding to spend a year away from his laboratory in order to write; but there is no doubt that he has done a most admirable and helpful thing, in setting down for us his results and thoughts after forty years work in muscle physiology. It happens all too seldom that a veteran in any field will make the effort to write down, let alone tidy up, the developments in his science throughout his lifetime.

He writes, understandably enough, with an intense sense of personal involvement. He evidently feels that his own contributions have been under-estimated and quotes with some bitterness "The publicity each theory has received has depended almost as much on the strength of personality of its protagonist as on its intrinsic merit".

Prof. Ernst's disputatious style, and his wide reading, combine to give a vivid historical picture of the way in which muscle physiology has developed. In addition, the experimental work for which he is best known—on the volume changes in muscle and on the osmotic activity of water in muscle—is presented in some detail; while numerous other aspects of muscle physiology are reviewed or discussed. Sometimes he does not give enough experimental detail to permit a firm answer to an important question, for example (p. 46), where he reports that isolated myofibrils are excitable electrically; and although some of his criticisms seem to me to be just—for example (p. 266), where he points to the confusion that surrounds the concept of muscular efficiency—he sometimes goes too far, or makes mistakes himself. Thus, in claiming priority over A. V. Hill for the discovery that when an active muscle is stretched it can absorb energy (pp. 11, 321), he seems unaware that his mechanical measurements alone, without heat measurement, cannot possibly solve this problem.

The book is well produced, but there is a cumbersome system of cross-referencing (to chapters and sections instead of to pages) that may have made it easier to write, but which certainly makes it more difficult to read. An infuriating example occurs on the last page (330), where it is implied that Hodgkin and Horowicz have failed to make proper reference to Prof. Ernst's work. To investigate this, a laborious search through the book is necessary, which ultimately arrives back on the self-same page from which it started, where it is found that the vital piece of evidence, by Laszlo, is still unpublished.

Nevertheless, it is Prof. Ernst's sincere interest in comprehending his subject that permeates and dominates his book. The fuel for his polemics seems to be the irritation that he feels because, after so many years work, by so many different people, the field still abounds in uncertainties, contradictions and misinterpretations.

D. R. Wilkie

INORGANIC MICRONUTRIENTS IN PHYSIOLOGY AND AGRICULTURE

Trace Elements

Proceedings of the Conference held at the Ohio Agricultural Experiment Station, Wooster, Ohio, October 14–16, 1957. Edited by C. A. Lamb, O. G. Bentley and J. M. Beattie. Pp. xii+410. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1958.) 12 dollars.

The volume under review comprises 23 chapters concerned with quite different aspects of trace-element nutrition, and a summary by Dr. C. A. Elvehjem given at a three-day symposium, which although rather unequal in treatment probably present in some respects more informed accounts than could be achieved by a single author.

Provocative contributions by Arnon dealing with the requirements and roles of trace elements with special reference to vanadium, molybdenum and manganese in different plant organisms, and by Hutner and his collaborators describing a novel approach to methods for revealing nutrient requirements by increasing metabolic stress with some emphasis on cobalt, present what may be termed the philosophy of trace-element investigations.

The chapters on selenium in soils, plants and animals by Moxon, on cobalt requirements by Davis, and on cobalt in B_{12} synthesis by Johnson and Bentley are both timely and informative. Iron is discussed by Granick, zinc by Hoch and Vallee, and copper mainly in relation to uricase by Mahler. Monoiodotyrosine metabolism is described by Serif and Kirkwood, but the use of bare references in place of certain details on methods and previous work are more akin to a paper of a series than a symposium contribution.

The specific role of boron in plant nutrition is still unknown. Skok, however, gives an excellently concise and detailed account of present knowledge regarding boron. Shorter papers by Sayre, and by McLean and Volk, deal with boron in corn and alfalfa.

Nason contributes a comprehensive statement regarding the roles of molybdenum and vanadium in plants and animals. The following paper by Keeler and Varner on molybdenum- and tungsten-protein fractions in *Azotobacter* approaches the problem of whether molybdenum fulfils a single or multiple role in *Azotobacter*.

The chapter by Pirson on manganese in photosynthesis reactions of higher plants and green algæ is a welcome summary regarding the apparent role of manganese in this complex process. Shorter papers discuss manganese problems in soils and in soybeans (Hoff and Medersky), manganese in grape production (Beattie), and manganese toxicity in apple (Winter).

Two chapters by Brown, Eyster and Tanner deal comprehensively with the mineral nutrition of *Chlorella pyrenoidosa* and especially with the differential effects of manganese in heterotrophic and autotrophic growth, respiration and photosynthesis. These papers, with those of Pearson, Arnon, Nason, Hutner and collaborators, Johnson and Bentley, and Keeler and Varner, comprise a fairly comprehensive account of micronutrient metabolism in micro-organisms.

Some minor omissions are of references to both sodium and chlorine in the index in spite of allusions in the text and the indexing of rubidium and fluorine. Reference to work of Brown and Possingham (1957) on iron and cell division is omitted from the text, pp. 378–9 and the index, though it is included in the bibliography, and the main paragraphs on hæmoglobin, pp. 368 and 370, are not indexed. The printing is excellent, and there are probably in all more than 1,000 different references conveniently distributed in relation to each chapter.

This book is recommended as a necessary part of any library used by students and teachers of plant physiology and of mineral nutrition in any field. Research workers will find therein much information on a wide range of trace-element problems and some stimulating or provocative points of view which may encourage further investigations.

E. J. Hewitt

Observation and Interpretation

A Symposium of Philosophers and Physicists. Edited by S. Körner in collaboration with M. H. L. Pryce. (Proceedings of the Ninth Symposium of the Colston Research Society held in the University of Bristol, April 1st–April 4th, 1957.) Pp. xiv+218. (London: Butterworths Scientific Publications; New York: Academic Press Inc., 1957.) 40*s.*; 8 dollars.

THE conference recorded in this volume brought together a remarkably distinguished international gathering of philosophers and physicists. There were seven sessions, at each of which two short papers were presented, and the discussion which followed was tape-recorded.

The main topic is indeterminism in quantum physics, with the problems arising from it. Several of the papers, including those of Profs. Braithwaite, Ayer and Popper, deal with the notion of probability, and discuss whether the frequency view is adequate for use within physics, and how to express the degree to which a belief is supported by evidence. The central argument develops with Profs. Bohm and Rosenfeld as antagonists, and leads to the question whether the laws of quantum mechanics would be the same whether there were human observers or not. Bohm outlines his view that the indeterminacy of quantum physics is not necessarily ultimate but may be explicable by deterministic behaviour at a deeper level, somewhat as random Brownian motions are explained by deterministic motions of molecules. Among the most interesting of the other papers are that of Prof. Körner on regulative principles in physics and that of Mr. Kneale on the question whether we can 'see' atoms.

Most of the papers could be read by anyone interested in the philosophy of science or in quantum physics. The discussions give the reader the excitement of a debate by experts on live and important issues. The volume is a successful experiment in the reporting of an important symposium.

E. F. CALDIN

Science in New Zealand

Edited by F. R. Callaghan. Pp. 272+27 plates. (Wellington, N.Z.: A. H. and A. W. Reed; London: Bailey Bros. and Swinfen, Ltd., 1957.) 22*s.* 6*d.*

AS with the British Association in Great Britain, it has become a tradition for the Australian and New Zealand Association for the Advancement of Science to issue a hand-book on the occasion of its periodical meetings. The holding of the thirty-second meeting in Dunedin in January 1957 was marked by the issue of the present volume. It makes no attempt to be comprehensive in its scope, and its articles aim at dealing with only a selected group of scientific interests. They are written in a style readily understandable by all readers and provide a general background knowledge of the scientific and cultural features of New Zealand.

A distinct local colour and flavour are regarded as an essential feature of an A.N.Z.A.A.S. hand-book and the present volume is descriptive, historical and scientific throughout its chapters.

Among articles of outstanding interest is one by Gilbert Archey on the relationships between Maoris and Polynesians, native and introduced birds by E. C. Turbott, geothermal power by G. W. Grindley, aerial top-dressing by E. A. Gibson, trans-Tasman relationships in natural history by C. A. Fleming, and the growth of hydro-electric schemes by F. R. Callaghan. There is also a valuable introduction showing the contributions made to the development of science in New Zealand by Sir Joseph Banks and Sir Joseph Hooker.

The book is well illustrated, not the least important photograph showing a group of Maori intellectuals considering the new edition of the standard dictionary of their language.

Micro-Organisms in the Soil

By Prof. Alan Burges. (Biological Sciences.) Pp. 188. (London: Hutchinson and Co. (Publishers), Ltd., 1958.) 10*s.* 6*d.* net.

FEW books have been written on soil microbiology since the Second World War, and therefore the present volume, although much biased towards soil mycology, will be most welcome to soil scientists. Workers in general in biological and related sciences should also find something to interest them.

Prof. A. Burges has taken upon himself a heavy task, and he is to be commended for approaching it from the ecological point of view. The opening chapter, which gives a brief account of the soil and its structure, is followed by a chapter on the various groups of organisms found in the soil. No diagrams or photographs are provided and consequently some of the descriptions of the more complicated organisms (for example, nematodes) and the systematics (for example, of the algae) will be fully appreciated only by those trained in zoology and botany. The succeeding chapters deal with such topics as: methods of examining the soil population; form, distribution and ecology of the organisms in the soil; the role of micro-organisms in the biochemical transformations taking place in soil; the influence of man on soil micro-organisms; and a consideration of soil as a dynamic equilibrium system. It is in these chapters that the true worth of the book will be found.

This volume will be very useful to students who have to learn something about soil microbiology and who are looking for an up-to-date account in a comprehensive form. The references at the end will be found of particular value in this connexion.

D. M. WEBLEY

A Treatise on Photo-Elasticity

By Prof. E. G. Coker and Prof. L. N. G. Filon. Second edition revised by H. T. Jessop. Pp. xxxvi+720. (Cambridge: At the University Press, 1957.) 70*s.* net.

THE Cambridge University Press has performed a very real service to all those interested in the theory and history of photoelasticity by producing a second edition of Coker and Filon's classic work on this subject; this was first published in 1931 and has been out of print for many years.

The book has been reprinted by the offset-litho process; it differs from the first edition, apart from a very few minor corrections and alterations, in only two particulars. The colour photographs contained in the original edition have been omitted, presumably to keep down the cost of the new edition, and the reviser, Col. H. T. Jessop, of University College, London, has added an excellent short introduction giving an outline of developments in the field of photoelasticity since 1931 and a short bibliography covering this period.

This new edition is a book which technological and scientific libraries as well as individual workers in photoelasticity will wish to place on their shelves.

E. K. FRANKL

THE NUFFIELD–WITWATERSRAND UNIVERSITY EXPEDITIONS TO KALAHARI BUSHMEN, 1958–59

By Prof. P. V. TOBIAS
Convener, Kalahari Research Committee, University of the Witwatersrand

DURING the winter of 1958 and the summer of 1959, two expeditions from Johannesburg carried out the most comprehensive series of field-studies ever made on the biology of the Kalahari Bushmen. The full collated reports will ultimately form the subject of a special monograph, but a provisional report on the background, organization and achievements of the investigation is presented here.

The Kalahari in Bechuanaland comprises a large area of sand veld, with slight rainfall, scanty vegetation, practically no agriculture, a sparse and often nomadic population and a virtual dependence of man on domestic and wild animals. It includes, too, the swamp-lands and broad rivers of the Okavango inland 'delta', which Prof. J. H. Wellington regards as potentially one of the chief food-producing areas of southern Africa.

The peoples of Bechuanaland fall into the following ethnic categories: (1) Bantu-speaking Negroids; (2) Hottentots; (3) Bushmen; (4) Europeans (Caucasoids); (5) Bastards—a variety of blends of the other four groups.

Of these five categories, the serious decline in numbers of the Bushmen over the past three hundred years, and especially in the last century, has made the study of this group the most urgent. Although recent estimates have placed the number of surviving Bushmen at as high a figure as 50,000 (Tobias, 1956), it has been deemed necessary for a number of reasons to give the highest priority to the Bushmen, in a systematic investigation of the inhabitants of the Kalahari. At present they are being subjected to rapid change in their conditions of life; to progressive blurring of their tribal boundaries in some areas, with consequent cultural and genetic detribalization; and to the impingement of other races, languages and cultures upon their genetic structure, click language and subsistence economy based on hunting and food-gathering.

For more than thirty years the Department of Anatomy of the University of the Witwatersrand has been studying the indigenous population of South Africa in general and the Bushmen in particular, especially the divergences in the skeletal structure of the Bush and Negroid peoples. These skeletal studies have been supplemented by a number of field-surveys over the past twenty years, as a result of which much information has been collected about living Bushmen (see, for example, Dart, 1937). Meanwhile, other studies had been devoted to linguistic, psychological, cultural and medical aspects of the Bushmen, as well as, in more recent years, their applied physiology. For many years, these field-surveys had been carried on in an unsystematic and desultory fashion.

Recent years have seen a considerable revival of interest in the physical anthropology of the Bushman and Hottentot peoples. As a consequence, no fewer than thirty-four papers bearing on this topic were published during the period 1952–55, compared with seven works in this category in the years 1948–51. Studies on the living have included physical and serological accounts of Nama Hottentots, Strandlopers, Koranas, Sandawe, Lake Chrissie Bushmen, Northern Bushmen, River Bushmen, Central Bushmen, and Bushman hybrids.

To co-ordinate and systematize the investigations, as well as to accelerate the work, in the face of rapid changes in the circumstances of the Bushmen, a Kalahari Research Committee has come into being at the University of the Witwatersrand. Its members are drawn from those departments of the University which have been concerned with the Kalahari researches, as well as from two collaborating institutions, the Applied Physiology Laboratory of the Transvaal and Orange Free State Chamber of Mines (director, Dr. C. Wyndham) and the National Institute for Personnel Research (director, Dr. S. Biesheuvel), a specialized institute of the South African Council for Scientific and Industrial Research.

The Kalahari Research Committee has initiated a systematic investigation of the inhabitants of the Kalahari Desert, among whom first place is being given to the Bushmen.

With the aid of a generous grant from the Nuffield Foundation, as well as substantial assistance from the University of the Witwatersrand and a grant from the S.A. Council for Scientific and Industrial Research, the Committee was able to mount the first two expeditions in August–September 1958 and January 1959.

The area selected was Ghanzi, where researches had previously been made on Bushmen (Tobias, 1955–56; Clement, Plotkin and Fosdick, 1956). Around the District Commissioner's camp at Ghanzi, and along a line of European- and Bastard-owned farms running westwards from Ghanzi to the border with South-West Africa, two major linguistic subgroups of the Bushmen meet: to the north and west are the much-studied Northern Bushmen of Dorothy Bleek, whereas to the south and east are the little-known Central Bushmen. The population studied on the 1958 and 1959 expeditions comprised predominantly Central Bushmen, with a smaller proportion of Northern Bushmen. All the branches of study represented on the expeditions were in the broad realm of human biology.

Physical anthropological studies. These were made by Mrs. H. Eriksen, of the Witwatersrand Department of Anatomy, and by Dr. J. S. Weiner, reader in physical anthropology in the University of Oxford. Very few measurements on Central Bushmen have hitherto been published, so the 150 anthropometric and anthroposcopic observations recorded on each of 86 adult males and 54 adult females constitute a valuable addition to knowledge. 81 of these individuals belong to the !ϰ5η (Magon) tribe, which has never previously been studied by physical anthropologists. 20 were of the Naron tribe, of which a small series had previously been published by Tobias (1955–56);

while 21 were Auen (Kaukau) of the Northern Bushmen. The remainder comprised mainly inter-tribal 'hybrids' and Bushman–Negroid hybrids.

For the first time on Bushmen, skinfold measurements were taken with a Harpenden skinfold caliper. The objective assessment of steatopygia and steatomeria was successfully attempted by measurement of skin pinches over the buttocks and thighs. The use of female investigators greatly facilitated this aspect of the work, since Bushwomen are always loth to uncover their buttocks, which are a much-prized feature in their sexual economy. Detailed measurements and observations could likewise be taken on the enlarged labia minora (macronympha or the 'Hottentot apron'). Dermatoglyphic records were taken on palms and finger-tips and will provide a useful basis for comparison with similar observations collected recently on Bantu-speaking Africans from Nyasaland, Tanganyika and the Zambezi Valley in Northern Rhodesia (unpublished results).

The study of skin colour by the old von Luschan tablet has long proved rather inadequate, and an excellent opportunity was provided for a more objective assessment by the use of Dr. Weiner's portable reflectance spectrophotometer introduced in 1951. He collected observations for the skin colour on the inner aspect of the arm and on the fore-arm, from 142 Bushman subjects. These readings will make it possible to specify quantitatively the range of skin colour and to compare this with that of other racial groups on whom the instrument has been used (including West Africans, South African Bantu-speaking Negroids and Australian Aborigines).

Blood-groups, hitherto not assessed on Central Bushmen, were investigated on 114 Ghanzi Bushmen. For the blood-grouping, Dr. A. Zoutendyk, of the South African Institute for Medical Research, has used almost the whole range of anti-sera of anthropological value, including the recently discovered 'negroid' Js and V anti-sera (supplied by Dr. E. Giblett, of Seattle) and the 'mongoloid' Diego (supplied by Dr. T. Layrisse, of Venezuela). The results, which have been published by Weiner and Zoutendyk in *Nature* of March 21, p. 843, confirm the generally negroid pattern of Bushman blood-groups, including the occurrence of V and Js. Diego antigen is totally lacking, while the previously established points of departure of Bushman blood from that of Negroids are confirmed, namely, high frequency of A and low frequency of B and the absence of Rh-(cddee).

Somatotype photographs, hair samples and hand-grip dynamometer readings were also collected by Dr. Weiner, while Mrs. Eriksen made plaster-face-masks of Bushmen to add to the collection of more than six hundred African life-masks built up by Prof. R. A. Dart and his assistants in the Anatomy Department during the past thirty years.

Oral and dental investigation. This was carried out by Dr. J. F. van Reenen, senior lecturer in the School of Dentistry of the University of the Witwatersrand. A clinical and morphological study was made of 278 Bushman dentitions. Nearly half the Bushmen examined had an edge-to-edge bite, generally with attrition. A high incidence of gingivitis and hypoplasia of the enamel was recorded, but the incidence of caries was low. In addition, a bacteriological investigation was made on samples of saliva from 41 Bushmen. First results indicated the presence of hæmolytic streptococci and of coagulase-positive staphylococci in a large proportion of subjects. Few were positive for yeasts and a fair number for lactobacilli.

Applied physiology. During the winter months of 1958, a team from the Applied Physiology Laboratory, University of the Witwatersrand, led by Mrs. J. S. Ward, investigated the physiological responses of Bushmen to cold. It was found that air temperatures ranged from 85° to 93° F. by day down to 29° F. at night. The difference between maximum and minimum temperatures on sunny days and clear nights might be as much as 50–60 deg. F. Relative humidity was low, and no condensation was recorded on any night. The theory has often been canvassed—not without challenge—that the Bushman is peculiarly adapted physically to life in the desert. Apart from the evidence adduced elsewhere (Tobias, 1957) that he is a late arrival on the desert scene, Mrs. Ward's team confirmed earlier observations by Wyndham and Morrison (*Nature*, 178, 869; 1956) that the Bushman's adaptation to Kalahari conditions is largely cultural, rather than anatomical or physiological. By the intelligent use of fire, shelter and individual bodily covering, the Bushmen create comfortable temperature conditions during the cold winter nights. Physiological indications are that Bushmen, like Europeans under these air conditions, suffer a fall in skin temperature and increase their metabolism by shivering.

In January 1958, a second team from the Applied Physiology Laboratory, under Dr. N. B. Strydom, studied heat responses of Bushman males to humid heat in a specially devised climatic tent. Pulse-rate, rectal temperature and loss of weight were recorded hourly during a 4-hr. stop-test in a saturated environment of 90° F.

The variable electro-cardiographic response of Africans on cooling of the precordium led Dr. B. Kaminer, senior lecturer in physiology, University of the Witwatersrand, to study with a portable cardiograph the records of 60 male Bushmen and to make precordial cooling experiments on 14 Bushmen. Arterial blood pressure readings on 102 Bushmen revealed no tendency for pressure to increase with age. In addition, water 'load' tests were made on 10 Bushmen and clinical examinations on 78 Bushmen.

Psychological performance testing. This was carried out by Dr. H. Renning, of the National Institute for Personnel Research, Johannesburg. His first problem, to determine whether the Bushmen are amenable to simple performance testing, could clearly be answered in the affirmative, and 86 males and 15 females were tested. The tests used were: (1) sand drawing; (2) pattern completion (coloured version); (3) object-relations test (Zilian); (4) Ishihara colour-blindness; (5) Müller–Lyer illusion (method of limits); (6) perceptual illusions (Herskovits *et al.*); (7) recognition of shape. Of these, only the Müller–Lyer illusion presented difficulties to the subject. All other tests, none of which required any verbal responses, appeared to give reliable results. Some tests requiring the handling of paper (for example, the 7-squares test) could not be used in the open, because of prevailing strong winds; and, in general, test sessions could not be extended beyond 40–50 min. without imposing an undue strain on the subject.

Although the evaluation of results will not be completed for some time, a few points can be made immediately:

(i) The intellectual capacity of the Bushmen tested varied over a wide range.

(ii) Personality and temperamental differences were also great and readily observable in responses to test situations. Emotional tension was marked in many subjects during the first 10–15 min. of the test session.

(iii) The ability to abstract is apparently little developed in the Bushmen. For example, whereas a simple alternation, in the object-relations test, of black/white/black/white, or square/round/square/round, was in most cases correctly continued when two pairs were presented, the series of black square/white square/black round/white round was found too difficult even when three complete cycles were laid out by the experimenter.

Dr. A. J. Clement, who led the expedition into the field and established its bases, collected further demographic data on the numbers and distribution of eight western Kalahari tribes. These data largely confirmed those collected earlier by Tobias (1956).

Nearly thirty years ago, Schapera (1930) wrote: "There seems little doubt that the Bushmen are steadily dying out as a race. What relentless persecution at the hands of other peoples has not achieved is being slowly accomplished by disease and racial intermixture. Racially pure Bushmen are already in a minority, and their ultimate absorption by their neighbours is probably inevitable".

Since then, though the factor of disease may have declined somewhat, intermarriage of the Bushmen with other peoples has continued apace under more settled conditions, so that both tribal and racial boundaries are rapidly becoming blurred. There is a distinct danger that the extinction of the Bushmen by hybridization is foreseeable and that, thereby, anthropologists will be robbed of the chance of gaining a most important insight into human development and adaptation. It is hoped that such a tragic default will be averted by the concerted survey launched by the Kalahari Research Committee.

THE MEDICAL RESEARCH REACTOR AT THE BROOKHAVEN MEDICAL RESEARCH CENTER

By Dr. E. E. STICKLEY
Medical Department, Brookhaven National Laboratory, Upton, Long Island, New York

After nearly five years of planning and more than two years in construction, the new Medical Research Center at Brookhaven is nearing full utilization as its unique Medical Research Reactor—the first in the world—has reached critical reactivity. This event occurred on March 15 at 9.44 p.m. New York time. The critical mass was established as 2·249 kgm. of uranium-235. Operation in the full power-range was achieved on April 3.

Since the design of the reactor was fully studied during the planning and testing stage, it is expected that the machine will come quickly into experimental use, bringing the new establishment nearly to a completely functioning state. The Medical Research Center buildings were dedicated on December 16 last, and the Research Hospital was transported from the old quarters as a unit and set up completely in its new space on January 6, while moving of the laboratories was completed in mid-February.

It is significant that this reactor is the first where every salient aspect of the engineering and design of the device was considered in relation to its use in the study of man and the diseases of man. Its conception and planning were an outgrowth of the pioneering investigations using the unequalled possibilities afforded by the large general-purpose reactor at Brookhaven, where the first experiments on neutron-capture therapy and medical applications of radioactivities of extremely short half-life were carried out. Eight years of experience with this reactor, gained through the extraordinary research flexibility of that device and the unstinted aid of its scientific, engineering and operating personnel, have prepared the way for further penetration into this unexplored region of medical-nuclear research with this newest tool.

Since the Medical Research Reactor was designed specifically for use in the research programme of the medical scientists on the Brookhaven staff, the initial decisions established the quality and quantity of neutrons required to advance the technology of the earlier medical experiments. The major requirements were an increase in the slow-neutron flux, better control over the energy of the neutrons, and improved clinical convenience. From a statement of the neutron requirements, a reactor core and reflector were specified, and around them appropriate special shielding was planned to permit the utilization of the greatest possible external neutron flux. Two shielded rooms have been built, one on either side of the reactor, separated from it only by a single wall. Vertically moving shutters of 20 tons weight have been installed to control the administration of the radiation. A smaller cell has been incorporated inside the shielding for studies of the whole-body effects of nuclear reactor radiations. Other experimental arrangements include tubes into the reactor structure for production of short-lived radioactive materials, as for use in therapeutic and diagnostic studies or activation analysis; the tubes are also adaptable for collimated neutron beams, which are of value in determining the penetration and energy changes of neutrons passing through tissue-equivalent materials.

The operational criteria were best met by a modified tank-type reactor in which the neutron moderation is supplied partly by graphite in sealed cans and partly by the natural water circulated for cooling. The core is further surrounded by a reflector of air-cooled graphite approximately 1 m. thick. Initially there are 17 fuel elements, made in the Bulk Shielding Reactor design, each fabricated from 18 thin laminated plates spaced to allow passage of cooling water. A total loading of 2·377 kgm. of highly enriched uranium-235 is used. Three safety rods, each worth 2 per cent of excess reactivity, are held by magnetic clutches;

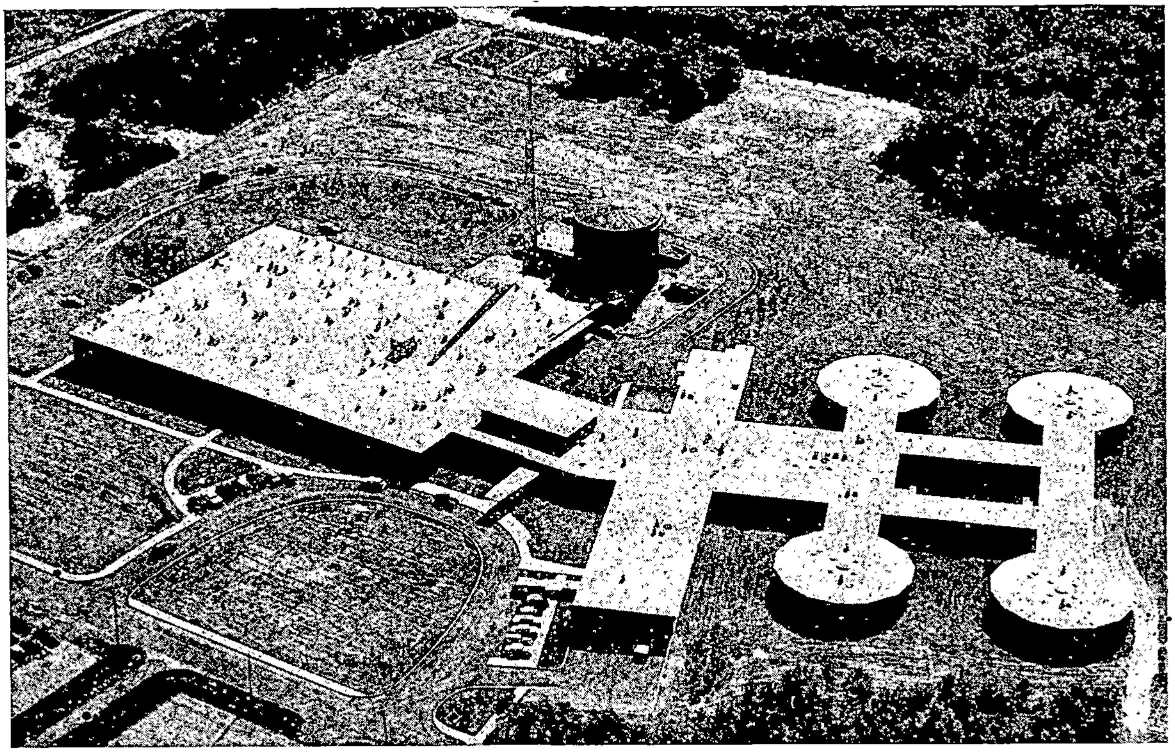

Fig. 1. Aerial view of the Medical Research Center. The reactor building appears above the centre of the picture. Research Hospital at the right. Industrial Medicine Clinic wing, lower centre. Medical Research Laboratories are at the left

they are driven into the core by gravity. Each consists of a stainless steel sheath with cadmium lining and boron carbide filling. A single control rod of similar pattern in solid steel, worth only 0·5 per cent in reactivity, is used for routine operation. At the nominal full power of 1 MW., the Medical Research Reactor is expected to have a core flux of 10^{13} and should deliver 7×10^{10} neutrons/cm.^{2}/sec. into the treatment room; this is twenty times the best flux previously available. Provision has been made for development of combinations of moderators, reflectors, filters and converter plates to select and modify the variety of radiations available in its several exposure sites.

Of these many uses and features of the Medical Research Reactor, three of outstanding immediate interest are: (1) the therapeutic application of high concentrations of slow neutrons delivered through the reactor shielding into a treatment room for the production of instantaneous radiation reactions, especially of the energetic heavy-particle variety; (2) the production of radioactive materials of very short half-life, to investigate their therapeutic and diagnostic possibilities; and (3) the development of more powerful analytical or diagnostic tests by the methods of neutron-activation analysis. In addition, other important applications lie in the use of the full range of reactor-produced radiations for studies of their comparative effectiveness in a wide variety of living systems and other materials of biological interest.

The Reactor is directly connected with the laboratories and the hospital through an air-lock corridor. To facilitate its use in the varied types of investigation for which it is expressly suited, a fully equipped operating room is adjacent, and treatment rooms for the application of high-level radioactive procedures are immediately at hand. The arrangements have been planned to eliminate any inconvenience in preparation or treatment of patients in carrying out the experimental procedures.

The Research Hospital provides a total of 48 beds in four circular pavilions, so arranged for the best control and convenience in observation and care; all the necessary additional service functions of a self-sustaining hospital are included. An Industrial Medicine Clinic occupies an adjoining wing, providing out-patient care and serving the occupational health needs of the Brookhaven National Laboratory as a working community. The Hospital and Clinic for handling patients are balanced by five related research divisions within the Department under the basic science headings of Physiology, Biochemistry, Microbiology, Experimental Pathology and Medical Physics. The nominal size of the scientific staff of the Medical Department is 48, all holding doctorates, two-thirds of them in medicine.

Research in clinical medicine and in fundamental laboratory medicine utilizes radiation both as a causative agent and as a label for constituents of living systems. Typical of this field is the intensive study of the relationships of radiation to blood dyscrasias. Radiation is used to induce disease for experimental study on one hand, while on the other, materials tagged with radioactivity are used to elucidate the natural history of the elements of the blood in comparison with their history under conditions of disease. It is of especial interest to note that efforts of the biochemists and the hæmatologists at Brookhaven to produce a radioactive substance which could deliver radiation selectively to the interior of cells did not bear directly the intended result, but

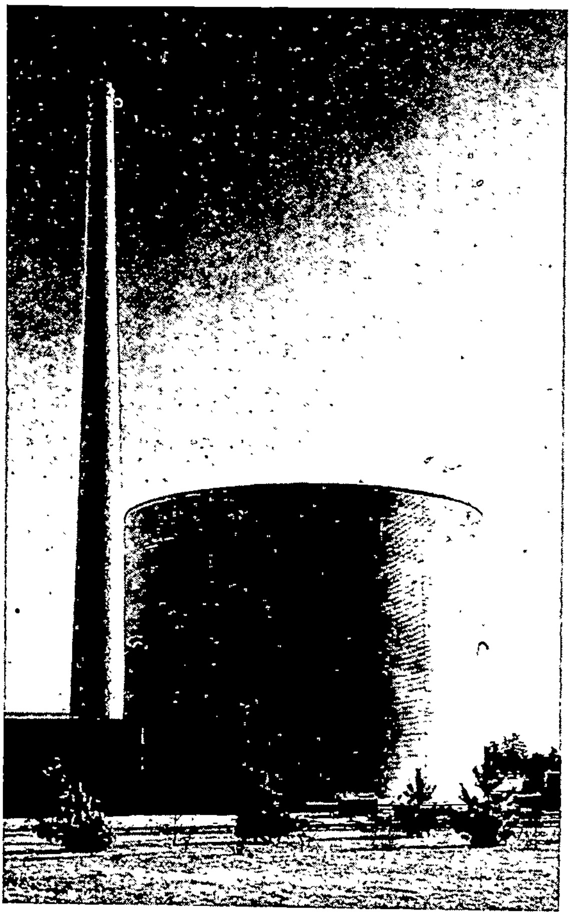

Fig. 2. Medical Research Reactor building. Cooling air for the reactor's graphite reflector is forced out of the 150-ft. stack. The steel reactor building, which is 60 ft. in diameter and 54 ft. high, is connected to the main medical research complex, where the hospital and laboratories are located

did unexpectedly provide one of the most valuable of biological tracers—tritiated thymidine—a tagged compound which immediately enters the cycle of blood constituents, appearing rapidly in large mononuclear cells of the peripheral circulation. Similarly, an attempt to develop a therapeutic application of a rapidly decaying radioisotope of manganese became an avenue opening up a broad investigation into the presence and the behaviour of trace metals in health and disease.

Much of the research programme and future planning are directed toward the special medical problems to be met in the coming nuclear age; novel tools are coming into use and are being used in various ways. Among Brookhaven's 'big machines', noteworthy use has already been made of the reactor; the high biological significance of neutrons of intermediate energy are being evaluated with a small cyclotron and a Van de Graaff accelerator; the large cyclotron has provided deuteron beams as well as rare radioactive isotopes from heavy-particle bombardment; the Hot Laboratory has searched for desirable radioactive materials of special metabolic properties. The collaboration of the scientific and technical staff at Brookhaven illustrates the co-operation which has stimulated and assisted the work of the Medical Department in its first ten years, as it grew into the present research establishment with its unique capabilities. The Medical Research Center is thus an integral unit in a scientific community of some four hundred scientists and engineers working on all the problems of the utilization of nuclear energy.

Brookhaven National Laboratory is a civilian establishment operated under the guidance of nine major universities of the eastern seaboard of the United States; they supervise its administration through Associated Universities, Incorporated, which makes contracts with the U.S. Atomic Energy Commission for supporting funds. The Laboratory is in the centre of Long Island, 70 miles east of the middle of New York City on a campus converted from the Army's former Camp Upton. In the years from its inception in 1947, as a result of the foresight of leading scientists in the new fields which research with the big machines opened up, Brookhaven has become familiar ground to hundreds of visiting and collaborating scientists from many foreign lands, all of whom have been welcomed for their contribution to the 'peaceful uses of the atom'.

The work described here is supported by the United States Atomic Energy Commission.

OBITUARIES

Prof. Arturo Duperier

Prof. Arturo Duperier, who recently died in Madrid at the age of sixty-two, was distinguished by his pioneer researches into the variation of cosmic-ray intensity with time and with meteorological conditions. He began this work in 1938 when he came to work with me and my cosmic-ray colleagues in the Physical Laboratories of the University of Manchester. Soon after the outbreak of the Second World War, when the cosmic-ray group largely dispersed for war activities, he moved his apparatus to the Imperial College of Science and Technology, London, where Prof. George Thomson gave him laboratory space. In a small room near the top of the Royal College of Science building at South Kensington, Duperier set up a cosmic-ray recording set and ran it almost continuously throughout the War and bombing, and for some years afterwards.

It was the results obtained from this long period of very precise recording of the cosmic-ray intensity which provided Duperier with the material for his analysis. His most important technical achievement was the introduction and use of multiple correlation methods for disentangling the origin of the observed variations of cosmic-ray intensity. In this way he was able to show quantitatively how the observed dependence of the cosmic-ray intensity on temperature might be an effect due to the decay of muons in the atmosphere. By careful use of meteorological data obtained from radio-sonde observations, Duperier was able to locate the average height of production of the muons as about 16 km. His method was to assume that the intensity varied both with the atmospheric pressure and with the unknown height of the muon-producing layer, and then to determine that value for the height of the layer for muon formation which gave the largest partial correlation coefficient.

This work demanded the meticulous analysis of a great amount of numerical data, at which Duperier was exceedingly expert. To facilitate this work he pioneered the use of business accounting machines for the analysis of cosmic-ray data. Later he refined his analytical method by introducing a three-term regression formula, and by this means obtained some indication—but no final proof—of the effect on the cosmic-ray intensity at sea-level of the pion decay in the upper atmosphere. This last work was carried out at Birkbeck College, where he moved soon after the War. In 1945 he gave the Guthrie Lecture to the Physical Society of London on the "Time Variations of Cosmic Rays".

Duperier was well known to cosmic-ray workers all over the world and regularly attended the biennial meetings of the International Cosmic Ray Conference, under the auspices of the International Union of Pure and Applied Physics, which has met since the War in Poland, India, France, Mexico and Italy. He will be greatly missed at the next meeting, planned for this summer in Moscow.

In 1951 Duperier returned to Spain, where he resumed his professorship in the Faculty of Science in the University of Madrid. The loss to his country of the most distinguished Spanish atomic physicist of his generation is indeed great. He was awarded posthumously the Juan March Foundation prize of 500,000 pesetas for his outstanding scientific work.

Throughout Duperier's thirteen years in England, I was in close touch with his work, and came greatly to admire him not only as a scientist but also as a man of unbending rectitude of character. It is thus both as a fine scientist and as a close personal friend that I mourn his death. P. M. S. BLACKETT

Prof. Pierre Fauvel

PIERRE FAUVEL, professor in the University of Angers, who died on December 12, was one of the greatest systematic zoologists. A specialist on Polychaeta, a group with which his name will for ever be associated, Fauvel was supreme in his field. No one who preceded him and none of his contemporaries approached the brilliance of his systematic interpretation.

Fauvel was born at Cherbourg on October 8, 1866. Throughout the greater part of his professional life he was on the staff at the Catholic University of Angers, as professor of zoology for fifty-three years, with a term of office as dean of the Faculty of Science from 1942 until 1947.

In the early stages of his career, 1894–1909, Fauvel worked on human physiology, publishing papers on digestion and uric acid secretion, and on general marine biology. In the latter field he carried out research on the larval development of *Arenicola*, on the circulation in Amphictenidae, on otocysts and on nephridia. For his doctorate of science he published observations made on the Ampharetidae. During 1910–20, however, the trend towards systematics becomes more apparent, and Fauvel's first major work in this field was on collections of polychaetes made in the Mediterranean and Atlantic during cruises of *l'Hirondelle* and *Princesse Alice*, under the direction of Prince Albert of Monaco. There followed papers on collections from the Falkland Islands, Australia, West Africa and Madagascar in this period, and all indicated that a new and brilliant figure had arisen.

With the publication in 1923 and 1927 of his two volumes in the "Faune de France" series, Fauvel's position as the outstanding authority on polychaetes was established. He provided in these works a practical method of identifying almost 900 species, his sedulous preparation of keys, in particular, being of the greatest value. In the genera *Harmothoë*, *Nereis* and *Serpula*, numerous species, previously a jumbled assortment of specimens and populations, were reduced to a series of well-defined natural groups as clearly delineated as available knowledge allowed. For those most difficult of families, the Phyllodocidae and Syllidae, his consideration of the species concept brought order out of confusion. This same ability to define species and clarify taxonomic problems is evident in all the families, so that these volumes have been in continual use in practical marine courses throughout the world since publication, and will probably not be replaced, even by local faunal publications, for years to come. Marine ecologists and physiologists everywhere praise their value and no specialist would consider approaching a problem concerning polychaetes before first noting what Fauvel had to say. In addition, these two works represent models of how the perfect faunal study should be presented, and their extension to other groups (and other areas for Polychaeta) is of paramount importance.

In 1932 Fauvel's work on the polychaetes from the Indian Museum in Calcutta was published, and this also is an invaluable guide to the student and specialist. It was the first comprehensive publication on polychaetes from subtropical and tropical waters, and has been the basis of all later diagnoses of the Indo-Pacific fauna.

Through experience with populations from widely separated regions, Fauvel was able to demonstrate the cosmopolitan nature of many species and the unique endemic elements in particular areas. He was the first to recognize the occurrence in Europe of *Mercierella enigmatica* as an invasion, possibly from India, of a species capable of breeding in waters of low salinity. Since then, repeated records of this polychaete from harbours in western Europe have indicated how damaging the effects of its growth might be.

Honours, richly deserved, were paid to Fauvel by his native France; they included: Chevalier de la Légion d'honneur; Lauréat de l'Institut, Prix Savigny de l'Académie des Sciences; Membre de la Société Zoologique de France; Membre Correspondant du Muséum d'Histoire naturelle de Paris. It is indeed with pride that systematic zoologists can point to the career of Pierre Fauvel, for he always upheld the finest traditions of learning in pursuing his chosen subject to the utmost of his ability, and he gave to zoology some of the finest products of scholarship published during his life-time.

NORMAN TEBBLE

Dr. Herbert Hunter

DR. HERBERT HUNTER died on February 21 at Meldreth, near Cambridge, at the age of seventy-six, after a long and productive working life, during which he had made outstanding contributions to plant breeding, to agriculture and to the malting and brewing industries. He will always be remembered for his activities in these fields, and also as a dedicated research worker and student of his subject who kept his interest in his work up to the time of his death.

Hunter graduated from the University of Leeds, of which he was a D.Sc., and started his researches into barley breeding in the early 1900's. This early work was conducted in Ireland, where he was head of the Plant Breeding Division, Department of Agriculture, Dublin, while he also became the first director of the Stormont Plant Breeding Station in Northern Ireland. Later, during 1936–46, Hunter was director of the Cambridge University Plant Breeding Institute. When in Ireland he bred the hybrid barley variety, Spratt-Archer, which was afterwards to make his name when it became one of the most successful varieties of cereals ever bred for Great Britain. It was introduced into cultivation in 1914, and has only been superseded as a standard malting barley in recent years. Hunter went to Cambridge in 1924, and he there bred two more varieties of barley—Earl and Camton—and a winter oat variety named Picton. All these varieties found a place in British agriculture and received official recommendation for farmers. Hunter's contributions gave him an established position with Sir Rowland Biffen and Dr. E. S. Beaven as successful pioneer plant breeders exploiting the new genetic knowledge.

This work ensured the recognition of Hunter's name nationally and internationally, but he also acquired a great reputation as a writer. He started contributing scientific papers and articles as early as 1908, and maintained a steady output throughout his life. He was an easy, lucid and fluent writer, and found an outlet for his talent in writing books, of which he had a number of successes to his credit. He wrote a standard work on oats, and one on barley in the 1920's, while in 1931 he edited a new edition of Baillière's "Encyclopædia of Agriculture" (with H. Martin Leake), while his most recent contributions were "Crop Varieties" (1954) and "The Barley Crop" (1956).

One of Hunter's great interests was the work of the National Institute of Agricultural Botany, to which he gave most valued service as a member of Council for twenty-one years, as acting director during the Second World War, and as chairman of Council for three years. For his services he was elected a vice-president of Council, a signal recognition of the way in which he guided the Institute's work and activities and established its present important relationships with agriculturists and commercial interests in the seed trade. Hunter's great tact, wisdom and kindliness were all instrumental in accomplishing this work so successfully, and those who worked under him in both Institutes which he directed were grateful for the experience.

In 1911 Herbert Hunter married Rosa Wise, of Springfield, Ohio. She died in 1945, and Hunter married in 1951 Mrs. Blanche Metters, widow of J. D. Metters. He is survived by his widow and two daughters of his first marriage. G. D. H. Bell

Dr. Alexander M. Cockburn

On February 28 Dr. Alexander Murray Cockburn, senior lecturer in geology in the University of Edinburgh, died at the age of fifty-seven.

Dr. Cockburn graduated with first-class honours in geology at Edinburgh in 1924. After a season with the Geological Survey of Canada, and some time spent in studying volcanic phenomena in Hawaii, he returned to his native city to take up postgraduate research as a Falconer Fellow of the University. In 1927, with John Mathieson, Dr. Cockburn carried out the first detailed topographic survey of the St. Kilda group of islands, and in the following year he completed a geological study of these islands, which was published in the *Transactions of the Royal Society of Edinburgh* in 1935, and remains a distinguished contribution to our knowledge of Scottish geology.

Dr. Cockburn was awarded the degree of Ph.D. in 1929, and was elected a Fellow of the Royal Society of Edinburgh in 1935. He began his long service as a member of the staff of the University of Edinburgh in 1931, and passed successively through the positions of assistant and curator of the museum, lecturer, and senior lecturer. In 1942, he took over from Prof. T. J. Jehu the courses in stratigraphy, and since then he was responsible for the formal stratigraphy courses in the Department. However, he never lost his early interest in vulcanology, and he made a comprehensive study of the volcanic rocks of the Pentland Hills. It is most unfortunate that his early death should have prevented him from publishing more than a small part of this work.

From 1951 onwards Dr. Cockburn acted as director of studies in pure science, and he was a member of the Senatus Academicus of the University of Edinburgh from 1956. A prominent Fellow of the Edinburgh Geological Society, he served as honorary secretary during 1939–44, and was elected president in 1958.

These few details of Dr. Cockburn's career can reveal little of the enormous debt which is owed to him by his Department and by all who have been associated with it. He combined a complete and unselfish loyalty to his subject and his Department with a deep and stimulating understanding of the personal problems of his students. He was a most able and conscientious teacher, both in the lecture room and in the field, and he carried a considerable administrative load. One of his great interests was the geological museum, and to this, and to the care of the Grant Institute building, he devoted a great deal of time and skill. Recently he has played a large part in the planning associated with a new building programme, and in the change from a three-year to a four-year honours course in geology. All the students who came under his care will remember with gratitude and affection the help and advice which he gave so readily, and his unfailing kindness, wisdom and good humour. All who were fortunate enough to know him feel a tragic sense of personal loss. F. H. Stewart

Dr. S. Bekku

By the death on September 19 last in Tokyo of Dr. S. Bekku, Japan has lost one of her distinguished electrical engineers.

Dr. Bekku was born at Ueno, Tokyo, in 1893, and he graduated in electrical engineering from the Tokyo Imperial University in 1917. After graduation he pursued advanced studies in the Electro-Technical Laboratory on electrical power transmission and high-voltage engineering. It was at this stage that Dr. Bekku had the opportunity of going to the United States and working with the Westinghouse Electric Company under the direction of Dr. C. L. Fortescue. In 1927, Dr. Bekku received the degree of doctor of engineering from the Tokyo Imperial University, and in 1928 he was appointed to a professorship in the Tokyo Institute of Technology. Here he lectured on transmission and high-voltage engineering. In 1931, Dr. Bekku took up an appointment with the Sumitomo Electrical Industries, where he was responsible for important research and development work in the field of electrical power transmission and distribution.

During the period up to the outbreak of the Second World War, Dr. Bekku published papers dealing with measurements on overhead transmission lines, unbalanced alternating current circuits, concentric cables and power capacitors.

In 1952, Dr. Bekku was elected president of the Institution of Electrical Engineers of Japan. In 1956, the Central Power Research Laboratory, a research association which serves the nine major electricity supply organizations in Japan, appointed Dr. Bekku its director and he was responsible for work on the development of the 380-kV. transmission system.

Dr. Bekku took great pleasure in the maintenance of his contacts with electrical engineers and physicists in the United States. He had travelled extensively in Europe and America and he enjoyed climbing and skiing. Dr. Bekku is survived by his widow, two sons and two daughters.

NEWS and VIEWS

The Rockefeller Foundation : New Officers

DR. J. GEORGE HARRAR has been elected vice-president of the Rockefeller Foundation. Dr. Robert S. Morison has been elected director for medical and natural sciences, a programme merging the biological, medical and public health interests of the Foundation. Dr. John C. Bugher is to be consultant on nuclear energy and as a principal officer will assist all programmes with respect to the impact of nuclear energy. Dr. Albert H. Moseman has been appointed deputy director for agricultural sciences, the new designation of the former agricultural programme. Dr. Lindsley F. Kimball continues as executive vice-president and Dr. Warren Weaver as vice-president for the natural and medical sciences.

Dr. Harrar joined the Foundation in 1943 as local director for the agricultural operating programme in Mexico. He became deputy director for agriculture in 1952 and director in 1955. Dr. Harrar is also serving in a special capacity as director of the National Academy of Sciences Survey on Education, Science and Technology in Africa south of the Sahara. When he joined the Foundation he was the sole staff of its agriculture programme. Established with Dr. Harrar's arrival in Mexico in 1943, this agricultural programme now has operating units in Mexico, Colombia, Chile and India, an extensive international fellowship and scholarship plan, and a grants programme in support of agricultural research and education. Approximately 6,270,000 dollars was appropriated last year by the Foundation in support of these three types of activities.

Dr. Morison was formerly director for biological and medical research in the Foundation. A graduate of Harvard University and of the Harvard Medical School, he taught in the latter before joining the Foundation in 1944. Dr. Bugher, a member of the Foundation's staff since 1943, was given leave of absence to serve for four years as director of the Division of Biology and Medicine of the U.S. Atomic Energy Commission. He returned to the Foundation in 1955 as director for medical education and public health. He represented the Atomic Energy Commission officially at the Geneva Conference on the Peaceful Uses of Atomic Energy in 1958 and is a member of the Commission's advisory committee on biology and medicine. Dr. Moseman joined the Foundation in 1956. He was previously director of crops research of the agricultural research service of the U.S. Department of Agriculture.

National Science Foundation Office of Social Sciences

THE National Science Foundation has recently established an Office of Social Sciences with Dr. Henry W. Riecken as its head. The Foundation has also appointed an Advisory Committee for the Social Sciences to advise on programmes and policy, the members of which are: Dr. Leonard S. Cottrell, social psychologist, Russell Sage Foundation ; Prof. Fred Eggan, professor of anthropology, University of Chicago ; Dr. John Gardner, president, Carnegie Corporation ; Dr. Pendleton Herring, president, Social Science Research Council ; Prof. Joseph Spengler, professor of economics, Duke University ; Prof. S. S. Wilks, professor of mathematics, Princeton University ; and Dr. Dael Wolfle, executive secretary, American Association for the Advancement of Science. The National Science Foundation intends to support basic research in the social sciences, since such support is invaluable in assisting social scientists to improve their research techniques, to accumulate fundamental knowledge about human behaviour and society, and to develop sound theoretical bases for further inquiry.

British Scientific Attaché in Moscow : Mr. D. A. Senior

MR. D. A. SENIOR, of the Royal Naval Scientific Service, has been appointed to the newly created post of scientific attaché to the British Embassy in Moscow ; he will advise the British Ambassador, Sir Patrick Reilly, on scientific matters and report on Soviet scientific and technical development in the civil field. Mr. Senior, who is thirty-five, will hold the rank of senior principal scientific officer and will be on the staff of the Department of Scientific and Industrial Research. Mr. Senior attended Batley Grammar School, Yorks, where he won an open scholarship to Trinity College, Cambridge. He graduated at Cambridge in 1943 with first-class honours in mechanical sciences (with distinction in electronics). He also won the Charles Lamb Prize in electrical engineering. In 1946 he shared the John Wimbolt Prize in civil engineering. From Cambridge he entered the Naval Construction Research Establishment at Rosyth, where he worked on high-speed photography. Since 1950 Mr. Senior has been at the Admiralty Research Laboratory, Teddington, mainly investigating problems of instrumentation and combustion. Recently, he carried out a study of acoustic methods of fish-finding. He has also been studying combustion on a part-time basis in the Chemical Engineering Department of the Imperial College of Science and Technology, London. Mr. Senior has a good knowledge of French, German and Russian. He is married and has three sons.

Peabody Museum, Yale: Prof. C. O. Dunbar

Prof. Carl O. Dunbar, who will retire from the directorship of the Peabody Museum at Yale on July 1, will then have served thirty-nine years on the faculty of Yale and sixteen years as director of the Museum. Prof. Dunbar graduated at Kansas in 1914 and obtained his Ph.D. at Yale in 1917. He was appointed assistant professor of historical geology at Yale in 1920 and then held various other geological appointments at the same University until he became curator of invertebrate palæontology and eventually director of the Peabody Museum. Dunbar is a palæontologist of international reputation and the author of many papers, and he has been editor of several scientific journals. His chief work concerned brachiopods and the Permian foraminifera. He is a Fellow of the Geological Society of London. His distinguished directorship of the Peabody Museum has been characterized by a wise and progressive policy.

Dr. S. Dillon Ripley

Dr. S. Dillon Ripley, a member of the faculty of Yale since 1946, has been appointed director of the Peabody Museum in succession to Prof. Dunbar. Prof. Ripley is an outstanding authority on birds, particularly those of the Far East, and is president of the International Council for Bird Preservation, an organization with sections in forty-five countries. Ripley graduated at Yale in 1936 and took his Ph.D. in zoology at Harvard in 1940. He served in the Second World War with the Office of Strategic Services, and was appointed to Yale as lecturer and assistant curator of zoology in 1946 and became associate professor in 1955. He has spent the major portion of the time outside the United States in the study of bird life. In several Asiatic areas he has been the first white man seen by the local population. He is also a distinguished writer and his works combine philosophy and literary quality with the recording of scientific facts. With such a background of experience the future of the Peabody Museum and its collections is assured.

The Argus High-altitude Geophysical Experiments

Dr. Alan T. Waterman, director of the National Science Foundation, and Dr. Detlev W. Bronk, president of the U.S. National Academy of Sciences, have issued a joint statement referring to the Argus high-altitude geophysical experiments last August and September. Reduction, analysis and evaluation of the observations have been going on, in order to interpret those of scientific significance. Plans are well advanced for the orderly distribution to the world's scientists of appropriate scientific information, as a part of America's participation in the International Geophysical Year. As scientific papers are completed, publication will proceed through the appropriate scientific journals. In addition, plans have been made to summarize the scientific results in the course of one of the four symposia to be held at the annual meeting of the U.S. National Academy of Sciences during April 27–29.

Atomic Power Station for Japan

The Japan Atomic Power Company has announced in Tokyo that on April 3 it had issued a letter of intent to the General Electric Co., Ltd., of England, for the construction of a 150-MW. atomic power station at Tokai-Mura, some seventy miles north-east of Tokyo. This order will be worth in the region of £20,000,000 and marks an important step forward for the General Electric Company, which has been reorganized into three main groups with the view of giving greater drive to its main activities, particularly the development of its heavy engineering and nuclear energy side. The success achieved in Tokyo has been accompanied by several other large engineering orders during the past month, including an order for two 200-MW. turbo-generator sets for the Kincardine station of the South of Scotland Electricity Board, valued at about £4,000,000, and an order for a complete ore preparation plant for the Redbourn Works of Richard Thomas and Baldwin, Ltd., valued at about £1,250,000.

Popularizing Astronomy

The International Geophysical Year and the launching of artificial satellites have led to a greater public awareness of scientific developments. This has created a need for the supply of accurate information in a more systematic manner than is possible in the average newspaper and with less technical detail than is appropriate even in an avowedly popular scientific magazine. The series of twelve articles which Dr. R. A. Lyttleton is contributing to the *Illustrated London News* is therefore especially welcome. Under the general heading, "The Universe at the Beginning of the 'Space Age' ", Dr. Lyttleton has written twelve articles. The first of these appeared on February 21, and the others are being published weekly in subsequent issues. The facilities provided by the *Illustrated London News* through their artist, Mr. G. H. Davis, are being used to great advantage in illustrating the articles. The first two articles dealt with the Earth and terrestrial meteorite craters. The next six deal with the Sun, planets, comets and the origin of the solar system, and the last four articles will deal with the universe of stars and galaxies.

Navigational Aids

In reply to questions in the House of Commons on March 18, asking for a statement regarding the recent meeting of the International Civil Aviation Organization at Montreal, the Minister of Transport and Civil Aviation, Mr. H. Watkinson, said that, in the Government's view, present standards of safety in congested air space could not be maintained with the use of VOR-DMET, the United States system of short-range navigational aid for aircraft, without seriously reducing the efficiency of air traffic control. Although twenty of the thirty-seven countries represented at the Conference voted for the adoption of this system, the British Decca system was the only navigational aid at present available which met the requirements of the International Federation of Air Line Pilots Association for an accurate and reliable short-range navigational aid based on the area coverage system, and designed to provide pictorial presentation of navigational information to the pilot in the cockpit. In the Government's view the Conference had not based its considerations on sound and objective grounds and the Government would continue to press for a more satisfactory solution. Mr. Watkinson hoped that the final decision, which vitally affected air safety, would be taken on proper technical grounds and not on grounds subject to pressure, national prestige or any other consideration than that of the safety of passengers in the air. Mr. Watkinson deprecated the lobbying that had occurred and agreed that, as neither system was fully proved, it would be wise to leave the decision for a period for further technical experience to be accumulated.

Research Associations

In answering questions regarding the British Hat and Allied Feltmakers Research Association in the House of Commons on March 17, the Parliamentary Secretary to the Ministry of Works, Mr. H. Nicholls, said that the Department of Scientific and Industrial Research had recently rejected the idea of a special grant to the Association in view of its development of No. 11 antishock felt in the production of protective caps for motorists and other road users. The Road Research Laboratory had been consulted by a hat manufacturer and had suggested that felt might be used in protective hats, and the manufacturer and the Research Association had co-operated with the Laboratory in selecting a quality, density and thickness of felt for antishock protection; but he stressed that such felt hats were no substitute for the motor cyclists' crash helmets, although they undoubtedly offered some protection. In reply to a further question regarding facilities in the Department of Scientific and Industrial Research for assisting in the choice of scientific instruments, Mr. Nicholls said that an instrument inquiry service is provided at the British Scientific Instrument Research Association and is largely financed by a contribution from the Association and an equal grant from the Department of Scientific and Industrial Research. Inquiries were at present running at the rate of 2,200 a year. The Research Association had a working party on instrument design which, *inter alia*, reviewed the specification, price and appearance of foreign instruments, and other research associations as well as the Department's research stations also designed new instruments.

Memorial Meeting to Prof. F. Joliot-Curie

A memorial meeting for Prof. Frédéric Joliot-Curie was held at Friends House, Euston Road, London, on January 22. It was attended by many scientists invited by the Association of Scientific Workers and by the National Committee of Science for Peace. The chair was taken by Prof. C. L. Oakley, president of the Association of Scientific Workers, and the speakers were Prof. C. F. Powell, Dr. Pierre Biquard and Prof. J. D. Bernal.

Prof. Powell outlined the contribution made by Joliot and his wife, Irene Curie, towards the discovery of the neutron, leading to the discovery, in 1934, of artificial radioactivity, for which in 1935 he received the Nobel Prize for Chemistry. Dr. Pierre Biquard, secretary-general of the World Federation of Scientific Workers and a close friend of Joliot's, described the joy Joliot had expressed to him at having been able to add to the contribution of French science to man's knowledge. Dr. Biquard also spoke about the part played by Joliot in the French Resistance during the Nazi occupation, when he refused to leave his country and stayed to help defend it after arranging for the valuable stock of heavy water to be brought safely to Britain. Prof. Bernal described Joliot's work on the international level. In the 1930's he had been a member of the Anglo-French Scientific Committee which had laid the basis for the foundation in 1946 of the World Federation of Scientific Workers, of which he became the first president. He had also taken an active part, as a representative of France, in the foundation of Unesco. Later, in 1949, Joliot was chosen as president of the newly formed World Council of Peace, a post which he held until his death.

International Journal of Radiation Biology

International Journal of Radiation Biology and related studies in Physics, Chemistry and Medicine is the full title of a new journal, the first issue of which is dated January 1959 (1, No. 1. Pp. 104. Subscription per volume (4 issues) 75*s*., post paid ; price per part 20*s*. plus postage. London: Taylor and Francis, Ltd., 1959). The editor is Dr. W. M. Dale, of the Department of Biochemistry, Christie Hospital and Holt Radium Institute, Manchester, and to assist him there is a large editorial board with distinguished representatives from Europe, the United States, Australia and Japan; regrettably, the U.S.S.R. is not represented. The first paragraph of the editorial gives a concise description of its aims: "In this new journal we propose to bring together all interests concerned with the biological effects of ionizing radiations. The field we hope to cover will not, however, be a narrow one, for it will embrace any discipline—medicine, physics and chemistry, for example—which has a bearing on our main theme".

The introduction of a new journal invariably arouses mixed feelings. We experience apprehension at the thought of having to add yet another publication to our check list, but on referring to this list, we find, rather surprisingly, that this new journal is the first primarily concerned with the important and growing subject of radiation biology. In the past there has been a tendency to regard radiation biology either as an appendage of radiotherapy or as a highly specialized version of applied physics. These views are completely unjustified and the practitioners of medicine and physics are necessarily joined by radiation chemists, biochemists, cytologists and geneticists in a combined attack upon a highly complex set of problems. The ten original articles in the first issue illustrate this clearly and embrace each of the above-mentioned disciplines. The international scope is revealed by the fact that these ten articles originate from no fewer than seven different countries. Articles may be submitted in English, French or German, accompanied by short summaries in all three languages; all articles in the first issue are, in fact, in English.

Publications in Microform

The problem of providing adequate storage space for the ever-increasing number of publications in science and technology is one that constantly haunts librarians. For journals which may be consulted infrequently and for books of historic importance some form of microform storage appears to be inevitable. The making of the most suitable types of microform materials itself raises problems of mechanics and storage and, for these and other reasons, librarians will welcome the enterprise of Micro-Methods, Ltd., of East Ardsley, Wakefield, Yorks, which has issued extensive lists of journals that have already been issued in micro-card, micro-film or micro-fiche form. Other lists contain details of rare and out-of-print books which have also been produced in microform. Among the many journals available are the *Journal of the Marine Biological Association* (1887–1913); the *American Journal of Psychiatry* (1921–50); the *Japanese Journal of Astronomy and Geophysics* (1922–47); *Jahrbuch über die Fortschritte der Mathematik* (1868–1944); and the *English Historical Review* (1886–1910). Rare books available in microform include Brongniart's "Histoire des Végétaux Fossiles", published in 1828, and Thumberg's "Flora Japonica", published in 1784. A series of theses from the Faculty of Metallurgy at the University of Sheffield is at present being prepared in microform. The charges of Micro-Methods, Ltd., appear to be reasonable and the company would welcome inquiries about the preparation of any publications in micro-form.

Anglo-American Library Associations

In Library Association Pamphlet No. 19, Mr. R. D. MacLeod gives a historical note on the beginnings of the Anglo-American Library Associations (pp. 15. London: Library Association, 1958. 2*s*.), which indicates that even eighty years ago the advantages to be reaped by co-operation were already evident. There is a useful bibliographical note, and apart from its historical interest the paper records an episode to which some parallel could be found a generation later in the matter of chemical abstracting.

University Library, Leeds

The annual report of the Librarian of the University of Leeds for the session 1957–58 (pp. 12. Leeds: Brotherton Library, The University, 1958) records accessions of 15,951 volumes, 3,306 pamphlets and 27,989 periodical parts, an increase of 11 per cent, bringing the holdings to 428,570 volumes and 173,311 pamphlets. Loans to readers totalled 101,220 and inter-library loans 6,041, the number of books lent increasing by 42 per cent. Keeping the library open until 10 p.m. proved an immediate success and has now been introduced on a permanent basis, but there was insistent pressure on seating accommodation and the staff position caused anxiety. The Nuffield pilot survey of library use was completed at the end of 1957 so far as the collection of material was concerned.

City of Leicester Museums and Art Gallery

The annual report of the Museums and Art Gallery at Leicester for the year ending March 31, 1958 (pp. 35+4 plates. Leicester, 1958), which is well illustrated, records difficulties in recruiting senior staff for museum work and also the completion of the reconstruction work on the roof of the main building. This had necessitated the re-designing of the natural history galleries on the first floor. The Schools Department has been able to increase the number of loans of museum material to schools, but the demand still outstrips the supply. A record was achieved in the number of temporary exhibitions shown, and the Saturday evening lectures maintain their appeal.

The Parliamentary and Scientific Committee

The annual report for 1958 of the Parliamentary and Scientific Committee (pp. 26. 1959), presented to the annual general meeting on February 18, includes a list of addresses and discussions held during the year. These dealt with the present and future position of the universities, with special reference to scientific and technological education and research; space satellites; latest developments with regard to the use of thermonuclear energy at power stations, with special reference to *Zeta*; the five-year plan for the development of China's agricultural resources; the work of the Department of Scientific and Industrial Research; veterinary science, its progress and application in Great Britain; international science; exploration in Antarctica, with reference to the International Geophysical Year; the research and development background to the railway modernization programme; and the medical problems of living in the nuclear age. Representatives of the Committee's Technical Education Sub-Committee discussed with the Minister of Education the question of future finance for colleges of advanced technology, and the Committee has also made representations on the appointment of a person with no legal or scientific qualifications as comptroller-general of the Patent Office, and is seeking further information about the disbanding of the Microbiology Group at the National Chemical Laboratory. A memorandum was submitted in May to the Pritchard Committee set up to consider the rating of charities and similar organizations including scientific societies, and in moving the adoption of the annual report on February 18, the chairman, Mr. R. Fort, said that the Committee and the Royal Society were the only organizations from which the Pritchard Committee took oral evidence; its report is expected early in 1959. Mr. Fort also referred to the way in which the Parliamentary and Scientific Committee could promote the integration of scientific disciplines, which he thought was the most probable line of scientific advance, and to the importance of maintaining varied sources for grants for scientific work.

Southern Regional Council for Further Education

The eleventh annual report of the Southern Regional Council for Further Education, covering the year 1957–58 (pp. 36. Reading: October 1958), records rapid progress in the development of technical education and steady growth of courses at all levels throughout the region. Regional procedure for considering proposals to establish new advanced courses operated smoothly and satisfactorily, while the record of developments in colleges in the area continues to be impressive. The Ministry of Education has now taken over from the Regional Council the annual publication of lists of sandwich courses available throughout Britain: List 182 details 263 courses being held in the session 1958–59, an increase of 65 on the previous session. Stress is laid on the importance of financial assistance in the development of such courses and on the need both for financial assistance from industry for its own employees and of co-operation between authorities and industry for others. Progress is reported in the establishment of formal and informal links between technical colleges and secondary schools in the area, and the Council has asked constituent authorities to agree to a new basis for arranging courses for technical teachers. At the request of the Council, the Regional Academic Board has begun a survey to assess the needs of industry in relation to the development of technical colleges, and attempts have been made to form an area group of the British Association for Commercial and Industrial Education. The Board has secured the presence of heads of grammar schools as members of advisory committees. A list of research projects and investigations carried out since 1955 in technical colleges in the region is included.

Science, Philosophy and Religion

THE Eddington Memorial Lectures have come to occupy a special place in the scheme of things, because they enable men of distinction to illuminate some particular facet of the working of that great mind. In his recent lecture entitled "Science, Philosophy and Religion" (pp. iv+31. Cambridge: University Press, 1959. 4*s.* 6*d.* net), Sir Russell Brain shows how the analysis of man, science and revelation, man and mechanization, perception and knowledge fit into the main stream of Eddington's thought; and this because the author is dealing with someone who was all at once Quaker, mystic, mathematician, astronomer and metaphysician. If one lesson emerges clearly from pondering upon Eddington's philosophy, it is that a new concept will be needed to enable us to explain total behaviour in a way which transcends individual components. This is well said for biological systems, but it (or something very like it) is becoming essential for inanimate phases, too, as witness the present discontents with 'classical' quantum theory. Ratiocination will try its hardest, though maybe these regions form part of the unseen world to which, as Eddington says, the human spirit must turn.

Design for Tropical Living

GROWING interest in the effects of environmental factors on life in tropical regions is to be found in the number of conferences and specialist meetings which have been held during the present decade. In 1951 an informal meeting was held in London to discuss co-operative research on building problems arising in hot climates. Unesco has organized two symposia, one held in New Delhi in 1952 to study the application of scientific principles, and one in Uganda in 1955 dealing with geographical factors in relation to the design of tropical buildings in the development of tropical Africa. The United States Building Research Advisory Board arranged a conference in Washington in 1953 on building in hot–humid and hot–dry climates, while in the same year, ecological problems arising from technical developments in tropical and sub-tropical countries were considered at an informal seminar held at Cambridge.

In 1955 medical and other aspects of African housing were considered at a conference under the ægis of the East African Advisory Committee for Medical Research in Nairobi. The Australian Academy of Science held a symposium in Brisbane in 1956 on man and his animals in the tropics, while in September 1958 the Scientific Council for Africa South of the Sahara arranged a specialists' meeting at Lagos on environmental factors affecting the physiology of man. The findings of these and other investigations were brought together during an admirable symposium arranged by the Natal Regional Research Committee of the South African Council for Scientific and Industrial Research and the University of Natal at Durban on October 18, 1957. The papers dealt with the climatic environment, deterioration of materials, physiological aspects of design for tropical living, psychological aspects of life in a warm climate, town and regional planning, climatic control by building, design, air conditioning in the tropics, and architecture in the tropics. These, and the ensuing discussion, have been published in a report (Symposium on Design for Tropical Living. Pp. vii+222. Pretoria, 1958) prepared by the National Building Research Institute of the South African Council for Scientific and Industrial Research.

Report of the Smithsonian Institution

THE annual report of the Board of Regents of the Smithsonian Institution for the year ended June 30, 1957 (cf. *Nature*, 181, 1709; 1958), has now been published as a bound volume (pp. x+499+74 plates. Washington, D.C.: Government Printing Office, 1958. 4.50 dollars) with a general appendix, including memoirs and reports of investigations made by members of the staff of the Institution or collaborators. Among those not previously published or not easily available may be mentioned E. B. Roberts's review of the United States Coast and Geodetic Survey, 1807–1957; Prof. T. Gold's James Arthur lecture, "Cosmic Rays from the Sun"; F. L. Whipple's "Meteors"; J. M. Chamberlain's "The Development of the Planetarium in the United States"; R. Lee's "Jet Streams"; E. B. Leopold and R. A. Scott's "Pollen and Spores and their Use in Geology"; Prof. R. E. Crist's "The Land and People of the Guajira Peninsula"; M. C. Leikind's "Aniline Dyes—Their Impact on Biology and Medicine"; and T. D. Stewart's "Stone Age Skull Surgery". A limited number of reprints of the papers are available on application to the Editorial and Publications Division, Smithsonian Institution.

Rand Corporation Publications

THE Rand Corporation has presented to the Science Museum Library, as a national deposit collection for Great Britain, a set of nearly 1,000 of its research publications. These range through mathematics, physics, electronics, aeronautics, economics, and the social and political sciences. They are now available for loan to all registered borrowers from the Science Museum Library, and to anyone as photocopies through the Science Museum Library Photocopy Service. The Index to the Rand Corporation Publications is held at the Science Museum Library, but is not for loan. Copies of the Index have also been deposited in the larger university libraries of Great Britain.

Design of Office Chairs and Tables

GENERAL principles which may be applied to the design of chairs and tables can be discerned in the results of a number of researches undertaken during the past few decades in several related biological fields. Studies of anatomical structure and function have given information as to where support for the body should or should not be provided. Clinical evidence demonstrates the results of insufficient attention to body mechanics. Studies of the times at which different muscle groups come into play and become fatigued in various activities, and the extent of their action in different positions, indicate the relative physiological efficiency of different working postures. Many anthropometric surveys have now been made with application to a wide variety of practical, industrial and military problems.

From these studies Dr. W. F. Floyd and Dr. D. F. Roberts have selected the findings relevant to the dimensions and design of office chairs and tables and summarized them in a report published by the British Standards Institution (Anatomical, Physiological and Anthropometric Principles in the Design of Office Chairs and Tables. B.S.3044, 1958. 5*s.* net). Among the factors considered are: posture, supporting the trunk weight, seat height, seat depth, seat width, tie rails, trunk stabilization, the backrest and table height. The report contains a bibliography giving details of previous studies in this and other related fields.

Fishing Gear of England and Wales

THE Ministry of Agriculture, Fisheries and Food has recently published a revised edition of the late F. M. Davis's "An Account of the Fishing Gear of England and Wales" (Fishery Investigations, Series 2, Vol. 21, No. 8. Pp. v+165. London: H.M. Stationery Office, 1958. 35*s.* net). Although a new edition of this standard reference work, now twenty-two years old, is to be welcomed, one can only regret that the opportunity has not been taken to bring it thoroughly up to date. Far too much of the book is taken up with descriptions of methods which are of interest only to the historian of fishing—methods which could equally well be found in a library copy of the earlier editions. This leads to an imbalance in the presentation. Thus the description of the Larsen trawl occupies no more space than that of the older (and much simpler) stownet which it has now almost entirely superseded, while the largely derelict fishing weirs, now only a memory to most fishing communities, receive fuller treatment than either. Despite, however, the resulting distortion of the overall picture of British fishing methods, the work remains an invaluable compendium of fishing practice around the United Kingdom.

The Wonderboom

THE famous wonderboom tree of Pretoria has been described as "the most remarkable example of its species in Africa and a National Monument". This magnificent 'tree' nestles against the sheltered north slope of the Magaliesberg range, a few miles north of Pretoria and close to the River Apies. The tree is an evergreen wild fig, *Ficus pretoriae* Burtt-Davy. There are many examples of this species in the district, especially along the northern base of the Magaliesberg range, and fine specimens have been recorded as far west as Marico. The best-known individual tree is the klein wonderboom, which is to be found a quarter of a mile to the west of Wonderboom Poort. The wonderboom is remarkable because of its mode of spread; no other example of this species has been found which has attained such considerable dimensions. The spread resembles that of the strawberry plant, the branches taking root with new trunks growing up until the single tree looks like a miniature forest. In the klein wonderboom thirteen 'individuals' have arisen from the original trunk. From north-north-east to south-south-west the diameter of the tree is about 170 ft. and from east to west about 145 ft. It is at least 74 ft. high. This famous banyan tree is described in a special issue of the *Transvaal Fauna and Flora* (No. 7; 1956), which is devoted entirely to the Wonderboom Nature Reserve.

Respiration of Excised Tomato Roots

IN a further contribution to our knowledge of the carbohydrate nutrition of tomato roots grown in pure culture, D. R. Morgan and H. E. Street have examined the sugars, and sugar phosphates and alcohols, which may serve as respiratory substrates (*Ann. Bot.*, N.S., 23, 89; 1959). The respiratory responses of substrate-depleted excised root tips to a range of sugars, sugar phosphates and sugar alcohols were determined by measuring oxygen uptake by the direct method of Warburg. Sucrose, dextrose and lævulose are the only sugars which promote a high level of oxygen uptake. The effects of azide and dinitrophenyl on the oxygen uptake promoted by sucrose and by dextrose are described. Mannose is a strong inhibitor of respiration. The inhibition is reversed by the simultaneous addition of those sugars which also reverse the growth inhibition caused by mannose. Mannose inhibits the respiration of sucrose and of glycolytic intermediates. Galactose is slowly respired and does not, even at high concentration, inhibit the respiration of sucrose.

Standards of Radioactivity

THE U.S. National Bureau of Standards Circular No. 594, entitled "Preparation, Maintenance, and Application of Standards of Radioactivity", by W. B. Mann and H. H. Seliger (pp. iv+47. Washington, D.C.: Government Printing Office, 1958. 35 cents), is a revision and unification of two review articles originally published in 1956 (*Internat. J. App. Rad. and Isotopes*, 1, 3 and 215; 1956). It surveys the current position in the field of standardization of radioactivity and describes the methods available for the preparation of both primary and secondary standards. The applications of the standards to problems in physics are discussed, including historical and geological dating from half-lives. One section is devoted to a summary of the results of the international comparisons of radioactivity standards which have been made during the past few years, and the circular concludes with an extensive bibliography. The main differences from the original articles are, apart from the inclusion of recent work, the use of a modified Harvard system of references and the incorporation of illustrations showing specifically the methods used at the National Bureau of Standards in the field of radioactivity.

Radio Industry Council Premiums for Technical Writing

THE Radio Industry Council has announced the award of six premiums of 25 guineas each for papers on radio and electronics published during 1958, as follows: "A New High-efficiency High-power Amplifier", in *The Marconi Review*, by V. J. Tyler (Marconi's Wireless Telegraph Co., Ltd.); "New Types of d.c. Amplifiers", Parts 1 and 2, in *Electronic and Radio Engineer*, by D. J. R. Martin (The Mining Research Establishment); "A Survey of Microwave Radio Communication", in *Electronic Engineering*, by W. J. Bray (Post Office Engineering Department); "All Travelling-wave Tube Systems", in *Electronic Engineering*, by S. Fedida (Marconi's Wireless Telegraph Co., Ltd.); "Electronic Developments at Very Low Temperatures", in *British Communications and Electronics*, by Dr. E. Mendoza (University of Manchester); "Analogue Computation", in *British Communications and Electronics*, by E. Lloyd Thomas (R. B. Pullin and Co., Ltd.).

Institution of Electronics Premiums

THE Institution of Electronics is to award the following new premiums for papers accepted for publication in the *Proceedings of the Institution of Electronics* during 1959: The Institution of Electronics Premium (25 gns.) for the most outstanding paper of the year; the Electronic Applications Premium (20 gns.) for the most outstanding paper dealing with the practical application(s) of electronics; the New Electronic Device Premium (15 gns.) for the most outstanding paper dealing with a specific new electronic device; the Institution of Electronics Exhibition and Convention Premium (20 gns.) for the most outstanding paper read at the 1959 Convention and accepted for publication in the *Proceedings*. Further particulars of the regulations governing these awards can be obtained from Mr. W. Birtwistle, Honorary General Secretary, Institution of Electronics, 78 Shaw Road, Rochdale, Lancs.

Carlsberg-Wellcome Travelling Research Fellowships

APPLICATIONS are invited for the Carlsberg-Wellcome Travelling Research Fellowships, 1959–60, the object of which is to encourage co-operation, on an exchange basis, between Danish and British research workers in any branch of the natural sciences which has a bearing upon human and animal medicine. One fellowship annually is awarded to a candidate from the United Kingdom for a year's work in Denmark and one annually to a Danish candidate for a year's work in the United Kingdom. The stipend is in the range £800–£1,200 per annum (or the equivalent sums in Danish kroner), travelling and some incidental expenses being provided in addition. Tenure of the awards will start in September, 1959. Inquiries from candidates in the United Kingdom should be addressed to the Assistant Scientific Secretary of the Welcome Trust, 52, Queen Anne Street, London, W.1. Completed applications must be submitted before April 30.

Institute of Metals: Officers

THE following were recently elected to office on the Council of the Institute of Metals: *President*, G. L. Bailey (director, British Non-Ferrous Metals Research Association); *Past-President*, Lord Tedder (chancellor, University of Cambridge); *Vice-Presidents*, Prof. H. Ford (Imperial College of Science and Technology, London); E. H. Jones (joint managing director, Capper Pass and Son, Ltd., North Ferriby); and Prof. H. O'Neill (University College of Swansea, University of Wales); *Honorary Treasurer*, D. P. C. Neave (director, British-American Metals Co., Ltd., Capper Pass and Son, Ltd., James Bridge Copper Works, Ltd., and Wolverhampton Metal Co., Ltd.).

Society for Analytical Chemistry: Officers

THE following have been elected to office in the Society for Analytical Chemistry for the forthcoming year: *President*, R. C. Chirnside; *Past Presidents serving on the Council*, J. H. Hamence, D. W. Kent-Jones, J. R. Nicholls, K. A. Williams; *Vice-Presidents*, D. C. Garratt, Magnus A. Pyke, J. G. Sherratt; *Honorary Treasurer*, A. J. Amos; *Honorary Secretary*, R. E. Stuckey; *Honorary Assistant Secretaries*, L. Brealey (*Programmes Secretary*), S. A. Price.

University News:

Belfast

THE following appointments to lectureships in The Queen's University of Belfast have been announced: Dr. A. H. Jarrett (applied mathematics); Dr. R. W. J. McCarroll (applied mathematics, digital computing); Dr. M. W. Roberts (physical chemistry); Dr. S. C. R. Dennis (engineering mathematics); A. M. Arthurs (engineering mathematics); B. G. Leary (electrical engineering).

Bristol

A GRANT of £2,075 from the Department of Scientific and Industrial Research to the Department of Physics for research in cosmic rays under Prof. C. F. Powell for the year ending July 31, 1960, has been received. The following have been promoted to senior lectureships from August 1, 1959: D. F. Gibbs (physics); Dr. R. J. Fitzpatrick (veterinary pharmacology).

Leeds

THE following appointments were recently made in the University of Leeds: Dr. A. Ralston, as temporary lecturer in the Department of Mathematics (Electronic Computing Laboratory); Dr. W. Rigby, as lecturer in the Department of Organic Chemistry; Dr. F. H. J. Cornish, as lecturer in applied mathematics.

Sheffield

THE following appointments were recently made in the University of Sheffield: Mr. C. L. Kirk, to be lecturer in the Postgraduate Department of Applied Mechanics; and Mr. M. Cable, to be lecturer in glass technology.

Announcements

DR. E. J. SOLVAY, of Brussels, has been appointed president of the Society of Chemical Industry in succession to Sir Robert Robinson, who will complete his term of office on July 10. Dr. Solvay is a direct descendant of the discoverer of the ammonia soda process which bears his name.

THE Langley Memorial Prize was founded by the friends of the late Dr. W. H. Langley, principal medical officer, Southern Nigeria, to commemorate his work and the services he rendered to Nigeria. The prize, of approximately £21, is open to officers, past and present, of the West African Medical Departments; it is awarded periodically for the best paper on one of the following subjects: (*a*) tropical medicine or surgery; (*b*) tropical hygiene and sanitation; (*c*) tropical entomology and parasitology. Entries for the award in 1959, consisting of either published or unpublished work, should be sent to the Dean, London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1, not later than October 1.

APRIL 22 is the twenty-first anniversary of the foundation of the British Coal Utilization Research Association. To mark the occasion the Association is throwing its laboratories open to inspection during April 22–24. On April 22, which is to be a private members' day, the proceedings will be opened by the Rt. Hon. Lord Mills, Minister of Power. Further information can be obtained from the Assistant to the Director-General, B.C.U.R.A., Randalls Road, Leatherhead, Surrey.

THE Clay Minerals Group of the Mineralogical Society is holding a meeting on Clay Minerals and Industry in Sheffield on April 15 and 16. Further information can be obtained from Dr. R. M. S. Perrin, School of Agriculture, The University, Cambridge.

THE X-ray Analysis Group of the Institute of Physics is holding a conference on Clay Minerals and Biological Fibres in the School of Chemistry, University of Leeds, on April 17 and 18. Further information can be obtained from the honorary secretary of the Group, Dr. R. C. Gordon, Safety in Mines Research Establishment, Portobello Street, Sheffield 1.

THE CARNEGIE INSTITUTION OF WASHINGTON

REPORT FOR 1957–58

YEAR BOOK 57 of the Carnegie Institution of Washington* includes the President's and departmental and administrative reports for the year July 1, 1957–June 30, 1958, together with a bibliography of publications. Reviewing the work of the Institution, the president, Caryl P. Haskins, recalls that the year marked the tenth anniversary of the dedication of the 200-in. Hale telescope on Mount Palomar and of the joint operation of the Mount Wilson and Palomar Observatories by the Carnegie Institution of Washington and the California Institute of Technology. Both the presidential and the departmental reports briefly survey the work of the decade and the important advances in knowledge, particularly in our ideas of the size of the observable universe, the magnitudes of the distances within it, and its age, and in our knowledge of stellar evolution.

During the year the magnetic classification and study of sunspots and related phenomena continued, and a series of direct photographs of the bright comet Mrkos (1957*d*) was obtained with the 48-in. Schmidt telescope. An extensive project on the chemical composition of stellar atmospheres is in progress and a survey of high-dispersion spectra of the early carbon stars has revealed differences in both the line and the band spectra. Coudé spectrograms with a resolution of 10 A./mm., or better, are being accumulated to obtain evidence bearing on mass loss from late-type giants and super-giant stars, and the investigation of the internal motion of nebulæ using the multislit technique and a dispersion of 4·5 A./mm. at the 200-in. coudé continued. Work on the colour-magnitude diagram of the Draco system showed that the diagram is of the same type as that of the globular clusters of the galactic halo and conforms to the rule that large numbers of cluster-type variables can only be expected if the horizontal branch on the red side of the variable gap is strongly populated. The direct photography of multiple galaxies continued, and also the investigation of objects which might be associated with radio sources. A theoretical investigation was conducted by the properties of the very luminous *OB* stars observed by Code and Houck, and a preliminary model of a photoelectric spectrum-scanning device was tried on the coudé spectrograph of the 100-in. telescope. The Committee on Image Tubes for Telescopes has continued to encourage the development of photoelectric image-intensifying devices for use in astronomy, directing attention both to methods that record the photoelectrons themselves and to methods that use photoelectrons to produce an optical effect.

The Department of Terrestrial Magnetism continued its study of the emission of energy at radio frequencies from celestial objects, but solar activity of unprecedented magnitude interfered seriously with optical red-shift measurements of the far-distant galaxies at Mount Wilson and Palomar, although work proceeded rapidly on precision equipment designed to measure the position of radio sources to within a few square minutes of arc. The density distribution and velocity distribution of atomic hydrogen gas clouds in our galaxy continued to be of major interest to the radio astronomy group, while three noteworthy projects were carried forward as part of the programme of the International Geophysical Year: the study of the intense band of electric current, called the electro jet, that circulates in the upper atmosphere in the region of the Earth's magnetic equator; a study of the Earth's crust in the Andean highlands at more than 200 sites, utilizing explosions normally set off in operating large open-pit copper mines; and the measurement of the ages of rock minerals through the methods provided by the study of radioisotopes, notably the geographical patterns of the ages of Precambrian rocks in North America, particularly the metamorphic Precambrian rocks of the central and southern Appalachians. A general picture of the geological history of the Appalachian orogenic belt has emerged.

The Geophysical Laboratory has constructed new equipment of rather revolutionary design for studying geochemical and geophysical phenomena: with a new 'single-stage' apparatus, pressures of up to 50,000 atmospheres at temperatures up to 1,700° C. have been achieved, and in the two-stage design, in which the piston of the single-stage apparatus is supported, up to 65,000 atmospheres at 1,100° C. The single-stage apparatus is being used to study the influence of pressure on the melting-points of minerals that might exist 80 miles below the Earth's surface. Work on mineral assemblages in the Green River formation, on the beneficial effect of potassium on soils contaminated with strontium-90, on the effect of water on the melting of silicates and on the biotites is reported in some detail, as well as work on feldspar, ore minerals of the sulphide type and on the diffraction effects of short-range ordering in layered sequences. In crystallography the magnetic structure of chalcopyrite has been determined by neutron diffraction studies and a crystallographic study was made of arsenopyrite by X-ray diffraction methods.

Five of the Institution's seven departments are concerned with biological investigations of one kind or another. The Geophysical Laboratory, for example, has investigated the detection of organic materials in Precambrian rocks and has significantly increased the yields of organic materials from processed shales such as Swedish Kolm shale (Cambrian), Nevadan Vanini shale (Ordovician) and Colorado Green River shale (Eocene). In the Biophysics Group of the Department of Terrestrial Magnetism attention has been focused particularly on the critical importance in metabolism and growth of the elaborate and precise fine structure of many of the constituents of the living cell. The properties of the ribosomes and the kinetics of their formation have been studied by ion-exchange columns, radioactive-tracer methods and the 'Spinco' Model *L* centrifuge. Work with *Escherichia coli* is described in some detail, while, besides studies on virus purification, extensive work on amino-acid analogues continued with particular emphasis on determining whether the analogues are contained in radically different molecular species or in proteins similar to those normally synthesized.

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* Carnegie Institution of Washington. Year Book No. 57, July 1, 1957–June 30, 1958. Pp. xi+497+12 plates. (Washington, D.C.: Carnegie Institution, 1958. 1 dollar, paper bound; 1.50 dollars, cloth bound.

Measurements in the Department of Plant Biology on the derivative absorption spectra of chlorophyll in numerous algae and other plants suggest that there are more than two forms of chlorophyll *a*. Further investigation on the photochemical formation of chlorophyll in leaves from its precursor photochlorophyll gave yields of about 0·5–0·7 molecule of chlorophyll formed per quantum of light absorbed, suggesting that two quanta of light may produce one molecule of chlorophyll. A study of the reversible oxidative bleaching of chlorophyll by chemical treatment and by light in several species of photosynthetic bacteria showed that the chemical properties of the pigment are markedly influenced by its incorporation in natural structures, the form absorbing light at the longest wave-length (890 mμ) being the most active. A number of climatic races of *Mimulus* plants are being grown for laboratory studies of the way their rates of respiration respond to variations of temperature and intensity of light, and studies have been commenced on the germination of seedling populations of contrasting parental and hybrid lines of *Mimulus* under crossed gradients of controlled temperature and light intensity.

In the Department of Embryology, studies of the molecular basis of rhythmic motility in spermatozoa indicated that the mechanisms of contractility and co-ordination can be disengaged experimentally. Important findings are reported in work on the development of the adrenals and sympathetic paraganglia in insectivores, and studies on the synthesis of the muscle proteins actomyosin and myosin in the regenerating limb of the salamander continued. Other work was concerned with differentiation and morphogenesis in the human embryo, the neural crest and its derivatives, the chemical basis of morphogenetic movements, the acquisition of biological specificity, the effect of hormones in developmental systems, and the anatomy and physiology of the uterus and the placenta.

In the Department of Genetics, studies with maize clarified an obscure aspect of the suppressor–mutator system of control of gene action, and analyses of biological ultrastructure by methods combining cytochemistry and electron microscopy offered new evidence that the chromosomes in actively dividing cells contain ribonucleic acids at all stages of the mitotic cycle. Studies of the intracellular deoxyribonucleases were concentrated on ascertaining the best procedures for extracting and purifying the intracellular deoxyribonuclease of salmon testes. Further studies of the properties of phage *T*2, which grows on strain *B* of *Escherichia coli*, suggest that phage particles are made from at least two protein sub-units, each containing a large fraction of the total phage sulphur. Studies of bacterial genetics with *Salmonella typhimurium* and *Escherichia coli* support the assumption that recombination among five genetic markers in the former is accomplished through a 'copy-choice' mechanism governing the exchange of characters between a recipient chromosome and a transducing element, and that the frequency of 'switchovers' in this process depends on the genetic constitution of the chromosome regions. Evidence has been obtained that transduction by bacteriophage lambda of loci concerned with galactose utilization in *E. coli* is a matter of lysogenization by a new type of genetic structure, which is part phage and part bacterial in origin.

The Department of Archæology completed its work during the year, and both the departmental and the presidential reports review broadly its work over more than fifty years. Some notes on ceramic studies in Yucatan and a ceramic technology are included in the departmental report.

THE NATIONAL RESEARCH DEVELOPMENT CORPORATION

REPORT FOR 1957–58

THE report of the National Research Development Corporation for the year ended June 30, 1958*, records a revenue from inventions of £174,242, notably from triiodothyronine, Prof. R. L. Wain's phenoxybutyric acid weed-killers, the Bailey bridge, the Royal Aircraft Establishment fire and heat detector and gyroscopic control apparatus for aircraft, the Ministry of Supply electrical ignition system and exploder, anti-thyroid compounds, the Hutchinson–Scarrott pulse height analyser, hecogenin from sisal, the Denny–Brown ship stabilizer control gear, nisin and anti-tumour agents of the nitrogen mustard type, on which all significant expenditure has ceased. Further reference is made to the Corporation's part in the development of electronic digital computers, including a project for the development of a large business-type computer and data-processing system of advanced design and performance, making extensive use of transistors, and two projects for magnetic type equipment for use with digital computers, but progress with the development of a very high-speed computer has been slow. An agreed programme of research and development of computer-controlled machine tools was initiated at the Manchester College of Science and Technology in January 1956, and interesting results are being obtained on the performance of slideways and on the cutting forces occurring during contour milling operations. Work continues on the development of high-performance drive systems, but the Corporation now considers that the time has come to withdraw its financial support.

Work at the National Physical Laboratory on Sir Thomas Merton's diffraction grating inventions is proving important in unexpected ways, and the Corporation's intervention in the development of printed electrical circuits has also been fully justified by results. The Corporation has now been able to retire from the collaborative effort it initiated seven years ago, leading to the collection of pituitary gland and production of adrenocorticotropic hormone on a commercial basis. Development of a process for producing aldosterone in significantly greater quantities from adrenal glands, including a limited amount of aldosterone and other adrenal hormones labelled with tritium, is also being financed, as well as a project for the isolation from *Pueraria mirifica*, from Thailand, of the œstrogenic substance, 'miroestrol', and elucidation of its structure, with the view of ultimate synthesis and medical use.

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* National Research Development Corporation. Report and Statement of Accounts for the year 1st July, 1957, to 30th June, 1958. Pp. ii+28. (London: H.M. Stationery Office, 1958.) 1*s*. 6*d*. net.

The four prototype groundnut harvesters shipped to East Africa in the spring of 1958 operated well on the true bunch varieties for which they were designed, but some difficulties were encountered in handling semi-bunch varieties, and commercial applications have been established for flexible barges of 40 to 1,000 tons capacity for transporting oil and other liquids by water. Among the new projects, some of which the Corporation proposes to attack under the extended powers confirmed by the 1954 Act, are a cotton-spinning project at the British Cotton Industry Research Association; a continuous-flow laundering project at the British Launderers' Research Association; a programme on ferroelectric ceramics at the Battersea College of Technology; the development of Prof. J. McGee's new form of image intensifier at the Imperial College of Science and Technology; the National Institute of Agricultural Engineering's jute ribboner; and an ultrasonic flow-meter at the British Scientific Instrument Research Association.

Government departments and research councils assigned patent rights in 86 cases compared with 105 in 1956–57, 49 of the total of 147 coming from the universities and eight from private firms and individuals in the United Kingdom, compared with 26 and 3, respectively, out of 148 in 1956–57. Of 612 inventions communicated to the Corporation during the year, compared with 631 in 1956–57, 231 were from Government departments and research councils, 13 from official organizations, four from charitable organizations and 286 from private firms and individuals, 265 in the United Kingdom. Holdings of British and foreign patent applications totalled 2,930, including 370 United Kingdom applications and 595 granted patents, 975 overseas applications and 990 granted patents.

FIGURAL AFTER-EFFECTS

PETER McEWEN'S monograph supplement to the *British Journal of Psychology*, entitled "Figural After-effects" (Monograph Supplement 31; 1958), is a timely summary of research and theorizing in a rapidly growing field of experimental psychology. The fundamental facts are relatively simple and universally accepted; they were first observed by the American psychologist, J. J. Gibson, who found that subjects who had inspected a curved line for some time would afterwards see a straight line as curved in the opposite direction. This discovery aroused relatively little interest until it was taken up by one of the great figures of psychology, Wolfgang Köhler, who had been one of the founders of the *Gestalt* school. He showed in a wealth of detail that almost any kind of visual or tactual perception produced certain effects of a relatively lasting character, effects which would change subsequent perceptions and which could be measured by the amount of such change induced. Most of his work was concerned with visual stimuli, but he also initiated experiments in kinæsthetic figural after-effect, and other sense modalities have also been studied since. It was Köhler who coined the term 'figural after-effects' by which these phenomena are now known.

Köhler did more than this, however. He proposed a physiological theory of the origin of these phenomena, making use of the concept of electrotonus, and deducing the observed phenomena from this theory. In recent years this has led him right over into the physiological field, where his vigorous and unorthodox approach has caused a good deal of discussion and criticism. Within the psychological field, however, he did one further great service by pointing out that his general theory could serve to explain many previously unrelated phenomena, such as the disappearance of certain visual illusions with time, and by suggesting that there were certain very striking similarities between the satiation process, which he believed to underlie figural after-effects, and certain inhibitory phenomena well known in the field of learning and conditioning. Köhler's theory therefore holds out an exciting prospect of unification of large areas of psychology which hitherto had been treated as quite separate from each other; this fact alone would justify the great amount of work that has gone into the testing of his hypotheses.

Dr. McEwen traces all this work, both on the experimental and theoretical level, in a painstaking, accurate and detailed account which is always judicious and remains close to the facts. He shows how much of the work that has been reported suffers from being purely phenomenological rather than quantitative, and how this lack of quantification has made any decisive type of experimentation or theorizing extremely difficult. To take but one example, after-effects are sometimes said to disappear after a few minutes, while at other times they are said to last for days or even months. McEwen also shows very clearly how complex the phenomena under consideration are, and how many of them require *ad hoc* hypotheses to be brought under the wing of Köhler's theory—or indeed that of the only rival theory, advanced by Osgood and Heyer.

It would probably be true to say that concentration on *apparently* unimportant issues and laboratory investigations of problems of theoretical interest characterize a maturing science, whereas exclusive preoccupation with direct practical questions is often characteristic of a pre-scientific stage. Similarly, the emergence of broad general theories covering a large amount of ground, and unifying many diverse phenomena, is also characteristic of a stage of relative maturity in a science, as compared with the purely empirical *ad hoc* investigation of unrelated phenomena. Learning theory was the first part of psychology to achieve such a level of maturity, and Köhler's work may now be said to have achieved the same status for perception. Indeed, the fact that he was able to point to very striking similarities between phenomena in perception and in the learning field suggests that an even greater unification may be in prospect. The whole situation is an exciting and promising one, and inevitably reminds one of those halcyon days in atomic research when interest was still confined to Bohr's model and Heisenberg's principle. The debt which psychology owes to Köhler had already been a large one before he investigated figural after-effects; his work in this field has almost certainly made him one of the greatest figures in psychology. It is curious and a little piquant to realize that the concepts which Köhler uses to account for figural after-effects are similar in many ways to those used by Pavlov to account for the facts of conditioning. That this should be so, in spite of the fact that not so very long ago Köhler and his colleagues founded the *Gestalt* school as an express antithesis to Pavlov's 'atomistic' and associationistic theorizing, illustrates the relative unimportance of the critical parts of the contribution made by schools in psychology, and the much greater importance of their positive and experimental contributions. We have fortunately now left behind to a large extent this era of rivalling schools, and it is fortunate that Köhler survived into and indeed partly originated this new period. The reader interested in the history of science can do no better than read through Dr. McEwen's monograph to discover both the promise of the present situation and also the severe birth-pains to which it is giving rise.

H. J. Eysenck

IRON ORE IN THE SOVIET UNION

"THE iron ore deposits of the Kursk magnetic anomalies, both as regards their concentration and their quality, have no rivals in the world"—so writes P. Y. Antropov, the Minister of Geology in the U.S.S.R. (*Priroda*, 7, 16; 1958). Magnetic anomalies were first discovered during a topographic survey in the region of Kursk in 1783. Before the 1917 revolution, E. E. Leist, professor in the University of Moscow, made a careful survey of magnetic anomalies and concluded that they are due to the presence of magnetite ores at great depths below the cover of sedimentary rocks. The results of the 1919–26 survey were rather disappointing; only rather poor iron ores were found and at a considerable depth. Renewed explorations during 1930–34 and the construction of an experimental shaft (flooded and ruined in 1938) revealed rich ore, but again at a great depth and in a very difficult geological setting. Exploration, on a much wider scale, was resumed after the Second World War. This detailed survey revealed two important features of the geological structure of this region:

(1) Below a cover, varying in thickness from 40 to 500 m. or more, the pre-Palæozoic floor revealed a gigantic anticlinal fold, or rather a packet of such folds forming a belt about 150 km. × 250 km. in extent stretching in a north-west–south-east direction, with the line Orel–Kursk–Belgorod as its diagonal. This pre-Palæozoic massif was buried under a cover of Palæozoic, Mesozoic and Tertiary sedimentary rocks, and was made of Proterozoic schists, ferruginous quartzites and gneisses.

(2) The rich iron ore was not found among the Proterozoic ferruginous quartzites but in a secondary iron ore formed as a crust of weathering immediately above the Proterozoic floor. This secondary iron ore was formed through an almost complete leaching out of silica from the ferruginous quartzites and a transformation of magnetite into martite (hæmatite pseudomorphs after magnetite). The maximum thickness of this ore deposit occurs in the Belgorod district, where it reaches 350 m. Elsewhere, it varies from 30 to 50 m. The best-quality ore occurs in the Yakovlevsky district, where it contains on average iron 61·4 per cent, silicon 5 per cent, sulphur 0·1 per cent and phosphorus 0·02 per cent.

The reserves of ores in the Belgorod region alone are 12 milliard tons, that is to say, five times the reserves of the Krivoy Rog iron ore deposit, until now the largest known in the U.S.S.R. The total reserves of the iron ores in the region of the 'Kursk magnetic anomalies' may be as high as 15–20 milliard tons.

The winning of these ores has already begun by means of shafts and open-cast quarries in the Lebedinsky, Mikhailovsky and Yakovlevsky districts. Thus in the Lebedinsky district the open-cast extraction amounted to 6 million tons in 1956; the Mikhailovsky district is planning to extract 6½ million tons per annum, and the Yakovlevsky district 15 million tons. Thus the total production of these three districts by 1966 is estimated at 27½ million tons per annum. These figures suggest that the total extraction of rich iron ore in the whole region may be estimated at 70–80 million tons per annum. This amount of ore would correspond to 30–35 million tons of cast iron per annum.

In this connexion it is important to note that in 1957 the total production of iron ore in the Soviet Union was 84·2 million tons and the total production of cast iron 37 million tons per annum.

S. I. Tomkeieff

EMPLOYMENT OF SCIENTISTS AND TECHNOLOGISTS IN THE UNITED STATES

ACCORDING to a preliminary report from the National Science Foundation, American industry in January 1957 employed 738,000 engineers and scientists (about two-thirds of all those in the United States), of whom 58,000 were employed as administrators of scientific and engineering activities. The largest occupational group was 528,000 engineers, chemists (72,000) coming next, followed by medical, agricultural and biological scientists (16,600), geologists and geophysicists (14,200), physicists (12,100), mathematicians (12,400) and metallurgists (10,800). Of the total, 92,900 were employed in the electrical equipment industries, 84,900 in the aircraft and parts industry, 79,200 in chemicals and allied products industries, 74,100 in machinery, 50,700 in petroleum products and extraction, 30,200 in fabricated metal products and ordnance, 29,500 in primary metals, and 24,600 in the professional and scientific instruments industry; 29,000 more chemists were employed in chemical industry than in any other industry.

Almost one-third (228,000) of these engineers and scientists were engaged in research and development, and two-thirds of these were employed in the aircraft, electrical equipment, machinery or chemical industries. Nearly three out of every five physicists, but fewer than one out of three of the engineers, mathematicians and biological scientists and two out of every five chemists were engaged in research and development. Nearly 600,000 technicians worked with scientists and engineers in all activities, and of these, 160,000 were engaged in research and development, the largest numbers in the electrical equipment, aircraft, machinery, chemical and fabricated metal parts and ordnance industries. During 1954–57 employment of engineers rose by 27 per cent, of chemists by 16 per cent and of biological scientists and physicists by about 60 per cent. In these three years 70,000 first degrees in engineering were awarded by American engineering; the proportion of engineers and scientists employed in research and development rose from 28 to 31 per cent, and employment in such activities rose by more than 45 per cent, whereas in the same period research and development costs rose from 3,700 million to 6,400 million dollars.

CHEMOTHERAPY OF PARASITIC DISEASES

A MEETING of the Parasitology Group of the Institute of Biology was held at the Institute's rooms in London on October 24, when two speakers were invited to read papers on the chemotherapy of parasitic diseases.

Dr. Ann Bishop (Molteno Institute, Cambridge) described some aspects of resistance to drugs in parasitic Protozoa. The fact that parasitic organisms can become resistant to drugs in the course of the therapeutic treatment of the host was discovered in Ehrlich's laboratory, early in the present century, by Franke and Röhl while studying the effect of parafuchsin upon *Trypanosoma brucei* in mice. Trypanosomes have since been made resistant to a wide variety of chemical compounds.

The fundamental problems in the study of resistance to drugs are the nature of the changes which organisms undergo in becoming resistant and the means by which these changes are brought about. In trypanosomes, resistance to drugs may be associated with changes in permeability and with changes in the enzymes present in the cells. Drug resistance in these organisms may be a very stable character and persists after the transmission of the parasite through the insect vector. The spontaneous development of resistance, in the absence of the drug, has been described both in trypanosomes and in *Toxoplasma gondii.*

Malaria parasites also can be made resistant to certain compounds, including proguanil and pyrimethamine, which are used in the treatment of the disease. Resistance persists after transmission of the parasite through the insect vector, in which, unlike trypanosomes, the malaria parasite undergoes a sexual cycle of development.

A study has been made of the development of resistance to metachloridine (2-metanilamido-5-chloropyrimidine) in pure lines of *Plasmodium gallinaceum* in chicks. No difference in the rate of development of resistance was observed in these lines. The rate of development of resistance was not related to the size of the dose of drug, but was affected by the size of the inocula producing the infections exposed to the action of the drug. The suddenness with which resistance appeared in some of the strains studied, and its stability in the absence of the drug and after the sexual development of the parasite, suggested that it arose by mutation, the mutation being of a low frequency.

Dr. O. D. Standen (Wellcome Laboratories of Tropical Medicine, London) outlined an approach to the experimental chemotherapy of helminthiases. The diseases of man and animals caused by the presence of helminth parasites are particularly important in the tropics, and are often responsible for the low level of efficiency and uneconomic production of stock animals in rural areas. The eventual control of these helminthiases will depend on a fuller knowledge of their epidemiology, but also presents problems which can only be resolved by the use of drugs.

The number of even moderately efficient anthelmintics in use at the present time is small, and most are toxic to the host. There is thus an urgent need for drugs which could be used in mass treatments of man and animals.

The discovery of new drugs requires the close collaboration of biologist and chemist. Two methods of approach may be used. An empirical method is one whereby large numbers of compounds of unknown activity are tested, in order to determine their effects on the parasite. The selective approach is one in which chemicals of known anthelmintic potency are modified in order to improve their action, and this method may be used with substances discovered by the empirical method. The ultimate aim is to discover the relation between the molecular structure of the drug and its anthelmintic activity and toxicity to the host.

The selection of helminths to be cultured in laboratory animals is of great importance. The number which can be cultured in this way is small, and of these the species pathogenic to man and animals are few. It is thus necessary to test drugs using helminths which are the natural parasites of laboratory animals. The successful maintenance of a parasite in all the stages of its life-history in laboratory animals often requires a long period of fundamental research before a sufficient supply of material is assured for routine investigations, for which an abundance of material is required since hundreds or even thousands of tests may be necessary before an effective drug is discovered.

The use of a multiple helminth screen, employing a wide range of species living in different habitats, yields interesting results. Thus, basic work with *Aspicularis tetraptera* in the mouse has contributed materially to the development of piperazine for the treatment of ascariasis and oxyuriasis. More recent chemotherapeutic tests, against *Nippostrongylus muris* in the young rat, provided the basis for the development of salts of bephenium that are efficient in the treatment of nematodiriasis in sheep and ancylostomiasis in man and dogs.

The experimental chemotherapy of helminthiases necessarily demands many species of helminths in all stages of their development and this offers an unparalleled opportunity for concurrent research into the structure and life-cycles of the parasites, into their biochemistry and host–parasite relationships and into the mode of drug action. While such studies may be an end in themselves, they also provide the only basis for a rational approach to chemotherapy.

In opening the discussion, Dr. H. O. J. Collier (Department of Pharmacological Research, Parke, Davis and Co., Ltd., Hounslow) said that the history of practical chemotherapy began with the treatment of parasitic diseases. Experimental chemotherapy also started in this field. In 1891 Ehrlich and Guttmann (*Berl. Klin. Wsch.*, 28 (9), 953; 1891) showed that methylene blue is a fairly potent antimalarial agent. Choosing this dye because it stained the malaria parasite within red corpuscles and because it was of low toxicity to man, Ehrlich, with Guttman's help, treated with it two sufferers from malaria and achieved immediate success. Later, Ehrlich had to test hundreds of compounds to achieve '606' and did not screen at random but approached his objective by steps, basing each new compound on results obtained with previous ones.

Work described in the preceding papers follows on the experimental chemotherapy started by Ehrlich. Each speaker was mainly concerned with one major problem, well known to Ehrlich and his colleagues; Dr. Bishop with resistance to drugs, and Dr. Standen with specificity of interaction between chemical and biological species.

Some of the ways in which drug resistance can develop were described. Compared with a sensitive organism, a resistant form may absorb a drug less, excrete it faster, destroy it more effectively, produce more of the drug's antagonist or possess a route of biosynthesis alternative to that blocked by the drug. These differences may depend on modifications of enzyme systems; an understanding of these would lead to a better understanding of drug resistance.

Problems of specificity are at the heart of chemotherapy, because if drugs were not more toxic to one species than to another, selective poisoning would be impossible. The differences in responses of various species to the same compound provide difficulties, however, because related species cannot be relied upon to respond in the same way to a new substance, and the second paper explained how the experimental chemotherapist deals with this dilemma.

Another aspect of the use of chemotherapeutic agents was mentioned by Dr. S. Kendall, in reference to coccidiosis of fowls. Drugs are added to feed in order to determine whether they are toxic to the parasite or whether resistance is developed. Results, so far, show these drugs to have a coccidiostatic action, without elimination of the parasite. Dr. L. Joyner said that this posed the general problem as to whether eradication of the parasite was necessary; in the case of flukes, for example, it was desirable. However, in some protozoan infections, it is preferable to induce a state of premunition in the host, or one of immunity induced by stages in the life-cycle other than the pathogenic one. Dr. J. Leiper said that some anthelmintics effective over a wide range may produce curious results, some parasites being killed and others encouraged. Thus, in the use of chemotherapeutic agents the habitat of the parasite within the host may be as important as the specific action of the drug. Dr. Standen replied that the range of activity of the drug must be carefully tested. Dr. C. Hopkins pointed out that the mode of action of the drug is unknown, a situation complicated by the difficulties of cultivation of parasites *in vitro*. Anthelmintics can act by blocking the metabolism of the worm, not necessarily causing a complete 'knock-out' reaction, and the site of the parasite within the host might indicate specific substances required from the host by the metabolism of the parasite.

The proceedings of this meeting will not be published in full. June Mahon

A PRESUMPTIVE HUMAN XXY/XX MOSAIC

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THE discovery of 'sex chromatin' by Barr and Bertram[1] and the subsequent recognition of its regular occurrence in normal females of many mammalian species (including man) has provided a new approach to the study of human intersexual conditions, the value of which is demonstrated in the proceedings of a recent symposium[2]. Although the presence of sex chromatin is generally taken to be diagnostic of an *XX* individual, this is not proved, and the unequivocal determination of the sex chromosome constitution can only come from the direct study of the chromosomes themselves.

A technique for obtaining chromosome preparations from biopsy specimens of bone marrow has recently been described in outline and used in the study of one 'chromatin-positive' case of Klinefelter's syndrome[3]. (Klinefelter's syndrome is a variable clinical syndrome in somatically male individuals who are sterile, generally with azoospermia, often with gynæcomastia and endocrine defects, but essentially and always with small testes after puberty.) The few cells from this first case seen in metaphase contained chromosomes indistinguishable from those of a normal female. Recently we have been able to examine the chromosomes from two further cases of this syndrome. One, chromatin-negative, had the chromosomes of a normal male. The second, chromatin-positive, gave an unexpected result and is the subject of this article.

A marrow specimen was obtained by sternal puncture at Guy's Hospital, converted into a suspension there and immediately sent to Harwell for cytological processing. The final preparations contained a satisfactory number of cells in mitotic metaphase, although many of them were unsuitable for accurate observation owing to supercontraction of the chromosomes, or separation of the chromatids at the centromeres, or both. Sixty-five cells were accepted as suitable for counting, and the results are summarized in Table 1. In ten cells, including those recorded as containing 48 and 49 chromosomes, there was an uncertainty of one, or two, chromosomes. The method of counting (to minimize subjective bias) and the errors to which the recorded counts are liable have been discussed previously[3,4].

Table 1. COUNTS OF CHROMOSOMES IN 65 CELLS. KLINEFELTER'S SYNDROME (CHROMATIN-POSITIVE)

No. of chromosomes	41	42	43	44	45	46	47	48	49
No. of cells	1	0	0	2	3	13	44	1	1

We have not yet succeeded in identifying the individual X and Y chromosomes, although it has been reported that Y is distinguishable from other similar chromosomes in preparations made from cells in tissue culture[5]. Nevertheless, it is possible to identify sex cytologically by classifying the chromosomes into four clearly defined groups[3]: (1) the shortest chromosomes have nearly terminal centromeres; there are four in the female, five in the male; (2) the next longer ones form a mixed group; there are sixteen in both sexes; (3) the medium-length chromosomes have sub-median or sub-terminal centromeres; there are sixteen in the female, fifteen in the male; (4) the longest ten chromosomes are well differentiated and form five easily recognized pairs that are the same in both sexes. It follows that Y is a short chromosome with a nearly terminal centromere and that X is a medium-length chromosome with a sub-median or sub-terminal centromere. This is in accord with observations on the sex chromosomes bivalent at metaphase in first spermatocytes[6].

Twelve of the cells with 47 chromosomes from the present case were selected for detailed analysis. All were found to contain five very short acrocentric chromosomes plus sixteen other short chromosomes (as in a male) and sixteen chromosomes in the medium-length group (as in a female). The remaining ten chromosomes were the five long pairs common to both sexes. An example is shown in Fig. 1. The obvious interpretation is that these cells contain two X-chromosomes and one Y-chromosome, in addition to the normal 22 pairs of autosomes, although the possibility that they are basically female and trisomic for one of the small acrocentric autosomes is not excluded. In so far as the 47-chromosome cells are concerned, our case is therefore parallel to that described very recently by Jacobs and Strong[7].

An attempt was made to classify the chromosomes in all thirteen cells with counts of 46. This was possible in eleven cells, although not all were of equal technical standard. Five of them contained an apparently normal female set with *four* small acrocentrics, sixteen other short chromosomes, sixteen medium-length and ten long chromosomes. There were points of uncertainty in the remaining six cells, but at least three of them probably had the same constitution. We therefore believe the case to be an instance of true mosaicism, notwithstanding the likelihood that some counts of 46 may represent damaged cells that originally contained 47 chromosomes. In the first place, there are many more cells with a count of 46 than would be expected (in our experience) from damage alone; and secondly, the chance of loss of one of the same group of five chromosomes from at least five, probably eight, and possibly more of the eleven cells must be very low indeed.

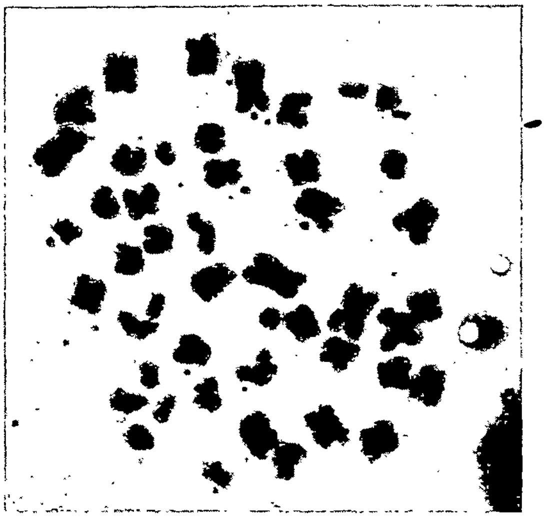

Fig. 1. Cell in metaphase with 47 chromosomes (presumptively XXY plus 44 autosomes) from the bone marrow of the patient with Klinefelter's syndrome (chromatin-positive). Feulgen squash after colchicine pretreatment. (× 2,220)

Granted that the 47-chromosome cells are XXY and the case is a true mosaic, it is most reasonable to suppose that the 46-chromosome cells arose through loss of the Y-chromosome by mitotic non-disjunction. It is known that clones of reticular cells, characterized by one or more visible chromosome rearrangements, may appear during the regeneration of the bone marrow in irradiated mice[8,9]; and recent evidence has shown that in certain circumstances they may proliferate differentially even to the extent that one clone is disseminated widely and outgrows all the rest (Ford, C. E., Micklem, S., and Gray, S. M., unpublished work). There is also evidence that marrow cells deficient in chromosome segments produced by irradiation of normal animals are very rapidly eliminated (Sharman, G. B., unpublished work). Now, loss of the Y-chromosome from an XXY cell would be a step in the direction of *normality*, and such cells might therefore exhibit a small selective advantage relative to their progenitors; on the other hand, loss of an autosome would yield a deficient cell, which, if it did not die, would not be expected to multiply. We therefore assume that the 46-chromosome cells contain two X-chromosomes and no Y-chromosome, that is, contain the normal female complement.

The supposition is that the mosaic patient developed from an XXY zygote and that this arose from fertilization of a non-disjunctional XX egg by a normal Y sperm, or of a normal X egg by a non-disjunctional XY sperm. The occurrence of one non-disjunctional type immediately suggests that others may be found. These could include XXX, $X0$, $Y0$, and possibly XYY types; some of them have indeed been postulated to exist on various grounds. Of these, perhaps, the most likely candidate is $X0$ for chromatin-negative cases of Turner's syndrome[10]. The occurrence of an individual with Klinefelter's syndrome and one with Turner's syndrome in the same sibship[11] is readily explained on such a basis, since the two syndromes would represent complementary zygotic types and could appear as a result of habitual non-disjunction of the sex chromosomes in a parent during maturation of either the ova or the sperm.

The *Drosophila* type of sex determination has been so frequently taken as a model in texts and reviews of all sorts that it is important to point out that in our case, and in the case reported by Jacobs and Strong[7], the *XXY* individual presented an essentially male phenotype, whereas in *Drosophila* the *XXY* fly is a fertile female[12]. If these cases should prove to be the first two instances of a general rule, it would indicate that the *Y*-chromosome in man is strongly 'male-determining', in contrast to the *Y*-chromosome of *D. melanogaster*, which is essentially inert in relation to the development of the sex phenotype, although necessary for male fertility[11].

We wish to acknowledge the skilful technical assistance of Mr. G. Breckon, Miss S. R. Wakefield and Miss P. A. Moore.

Addendum. Since the draft of this communication was completed, we have, in conjunction with our colleagues, Dr. D. G. Harnden and Dr. K. W. Jones, examined the chromosomes of three more chromatin-positive cases of Klinefelter's syndrome and of one chromatin-negative case of Turner's syndrome. The former all have 47 chromosomes, show no evidence of mosaicism and are presumptively *XXY* individuals. Forty-five chromosomes were found regularly in bone marrow cells from the patient with Turner's syndrome, and analysis of the detailed chromosome morphology is consistent with the anticipated *X*0 constitution. (Miss Jacobs and Dr. J. S. S. Stewart have kindly allowed us to state that they have found 45 chromosomes in a chromatin-negative case of Turner's syndrome, and that their observations are also consistent with *X*0 interpretation.)

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TRANSPHOSPHORYLATING ENZYMES AND MUSCLE RELAXATION

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THE pure creatine phosphate or the phosphoenolpyruvate kinase system greatly enhances the reversible relaxation of glycerinated rabbit muscle[1] (fibre bundles or single fibres) after contraction with adenosine triphosphate[2-5]. Transphosphorylation (presumably to adenosine diphosphate), though essential, is by itself insufficient to cause relaxation of old or specially extracted fibres. In such cases, in addition, the presence of a microsomal (or granular) fraction from muscle homogenate is required for relaxation. This has been demonstrated for the isotonic condition with creatine phosphate[6-8], and for isometric relaxation in conjunction with phosphoenolpyruvate[4,5].

Although the role of the microsomal principle for relaxation is generally accepted, the function of the transphosphorylating enzymes is regarded by many as 'unphysiological'[9-13]. It is claimed that the need for transphosphorylation arises only if the penetration by diffusion of adenosine triphosphate into the fibres cannot match the hydrolysis of the nucleotide by the myofibrillar adenosine triphosphatase. The addition of an enzyme system which restores adenosine triphosphate would merely ensure that the interior of the fibre maintains the necessary level of adenosine triphosphate similar to that prevailing in the bath in which the fibre is immersed. These contentions are based mainly on the work of Weber and his collaborators, and that of Bendall, who could not demonstrate any need for the addition of transphosphorylase in Marsh's system[14] in which, instead of fibres, homogenized myofibrils of microscopic dimensions are used. The experiment can be per-

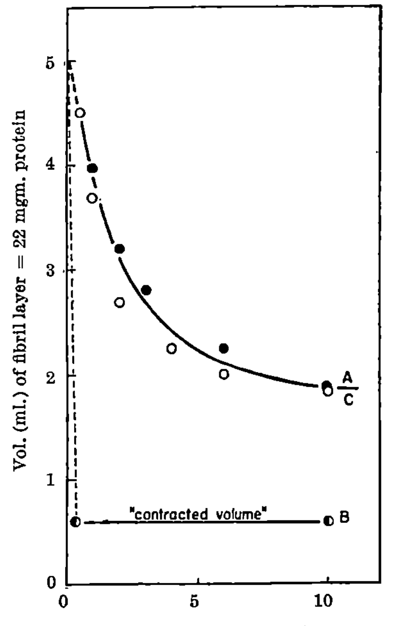

Fig. 1. Sedimentation of myofibrils. Magnesium chloride, 4 m*M*; *p*H about 6·5; $\mu \approx 0·15$; total vol., 5 ml.
A, fibrils (about 22 protein-mgm.—ref. 15) alone; *B*, fibrils + (1·04 protein-mgm. microsomes + 2·6 m*M* phosphoenolpyruvate—ref. 16) or (microsomes + 180 µgm. phosphoenolpyruvate kinase—ref. 17) + 4 m*M* adenosine triphosphate; *C*, fibrils + microsomes + phosphoenolpyruvate + phosphoenolpyruvate kinase + adenosine triphosphate

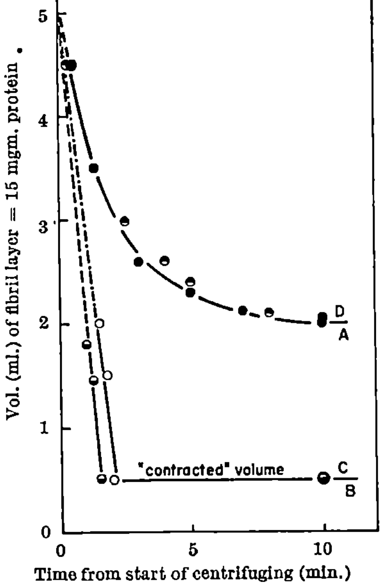

Fig. 2. Sedimentation of myofibrils. Conditions same as in Fig. 1. *A*, fibrils (about 15 protein-mgm.) alone; *B*, fibrils + 4 m*M* phosphocreatine (ref. 18) + 20 µgm. creatine phosphate transphosphorylase (ref. 19) + 4 m*M* adenosine triphosphate; *C*, fibrils + 1·52 protein-mgm. microsomes + adenosine triphosphate; *D*, fibrils + microsomes + phosphocreatine + creatine phosphate transphosphorylase + adenosine triphosphate

formed either by observing the packing volume of the myofibrillar layer during sedimentation in a low centrifugal field, or by measuring under the microscope the unloaded shortening of individual fibrils. The prevention of the mechanical change induced by adenosine triphosphate is generally assumed to be a phenomenon similar to relaxation.

In the present communication we wish to report that transphosphorylation is a very sensitive regulator of muscle 'relaxation' even in the Marsh experiment. This is noticeable particularly if the transphosphorylating enzyme systems are used in conjunction with such minimal amounts of microsomal component as would produce alone scarcely any effect. Figs. 1, 2 and 3 show this striking potentiation by the creatine phosphate and phosphoenolpyruvate kinase systems for inhibiting contraction. During centrifugation at about 1,000 r.p.m., at room temperature, the volume of the myofibrillar layer was measured with the aid of stroboscopic light. In Fig. 3 the results are presented in a somewhat more representative fashion. Fractional 'relaxation' (Q) is defined in terms of the volumes of myofibrillar layers as:

$$Q = \frac{V - V\,(\text{contracted})}{V\,(\text{standard}) - V\,(\text{contracted})} \times 100 \qquad (1)$$

where V represents an experimental volume at time t, V (standard) is the volume at time t of myofibrils sedimenting without the addition of adenosine triphosphate, and V (contracted) stands for the final volume of the myofibrillar pellet sedimented in the presence of adenosine triphosphate. It will be seen that values of Q less than 100 indicate contraction, and it can also be noted that both the creatine phosphate and phosphoenolpyruvate kinase systems prevent changes in volume very effectively under the experimental conditions described. Though not shown on the graphs, we have further demonstrated that the extent to which contraction is inhibited appears to be, within certain limits, a function of the concentration of phosphagens and their enzymes. Actually, by selecting appropriate conditions, Q values considerably greater than 100 can be obtained, which signify a swelling of the myofibrils.

Since lowering of the myofibrillar adenosine triphosphatase activity appears to be a characteristic symptom of the relaxed state in muscle (see, for example, ref. 13), we have studied the rate of hydrolysis of adenosine triphosphate by the myofibrils in the presence of various combinations of the microsomal component and transphosphorylating enzyme systems. Fig. 4 illustrates the finding that adenosine triphosphatase, though not suppressed by the concentrations employed of microsomes or transphosphorylase and phosphagen alone, is effectively reduced if they are all present simultaneously.

The myofibrillar material used in these experiments was obtained by homogenizing minced rabbit muscle with 0·15 M potassium chloride (buffered to about pH 6·8 with potassium salts of veronal and acetate) for 3 min. in the cold in a 'Virtis' homogenizer at 30,000 r.p.m. After centrifuging at 3,000 r.p.m., the light upper fibrillar layer was separated from the cell debris and was resuspended repeatedly (6–10 times) with the aid of the homogenizer and washed in buffered potassium chloride. In many instances, the fibrils were stored at − 20° C. in 50 per cent (v/v) glycerol and washed again in potassium chloride several times before use to eliminate the glycerol.

The microsomal component was isolated from the muscle homogenate as the fraction sedimenting between 11,000 and 54,000g, after the elimination of the inactive sediment obtained during centrifugation at 11,000g for 30 min. The microsomal fraction was resuspended in potassium chloride with

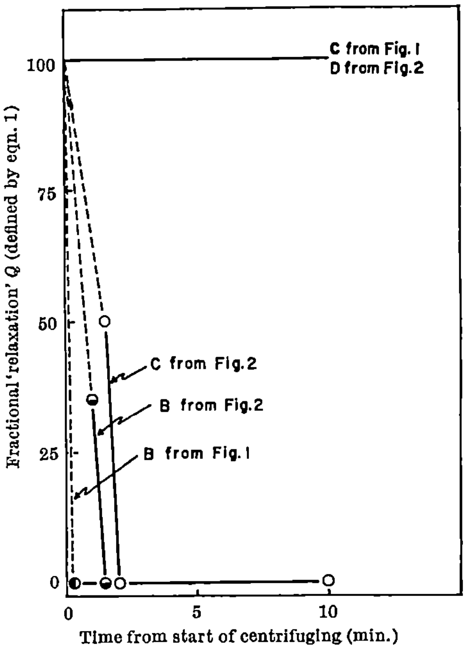

Fig. 3. Inhibition of the adenosine triphosphate-induced contraction of myofibrils by the creatine phosphate and phosphoenolpyruvate kinase systems. For explanation see text

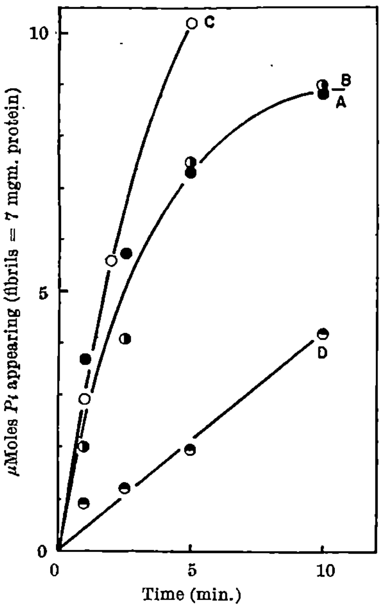

Fig. 4. Reduction of myofibrillar adenosine triphosphatase under the joint influence of microsomes and the phosphoenolpyruvate kinase system. Inorganic phosphate was measured by the method of Fiske and SubbaRow (ref. 20). Reaction mixture of 2·5 ml. at 25° C.: *p*H 6·5; $\mu \approx 0 \cdot 15$; 4 m*M* magnesium chloride; 4 m*M* adenosine triphosphate; about 7 protein-mgm. myofibrils. *A*, fibrils alone; *B*, fibrils + 1·19 protein-mgm. microsomes; *C*, fibrils + 0·35 protein-mgm. microsomes + 2·5 m*M* phosphoenolpyruvate + 150 μgm. phosphoenolpyruvate kinase; *D*, fibrils + 1·19 protein-mgm. microsomes + 2·5 m*M* phosphoenolpyruvate + 150 μgm. phosphoenolpyruvate kinase

the aid of a Potter hand-operated ground-glass homogenizer and centrifuged as before. This washing procedure was repeated several times.

In conclusion, the experiments presented here show that the interaction of the microsomal component of muscle with a transphosphorylating system is an essential feature of relaxation.

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MECHANISM OF ACTION OF DIPHOSPHOPYRIDINE NUCLEOTIDASES

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MAMMALIAN diphosphopyridine nucleotidases of the glycosidase type were first clearly described, as enzymes that inactivate coenzyme 1, by Mann and Quastel[1]. These workers demonstrated the inhibitory action of nicotinamide upon the reaction catalysed by diphosphopyridine nucleotidase. Later, Handler and Klein[2] showed that the enzymic breakdown of coenzyme 1 by tissue debris is accompanied by liberation of nicotinamide. The work of McIlwain *et al.*[3] established that this degradation of coenzyme 1 is accompanied by the conversion of a quaternary nitrogen structure to a trivalent one with the concomitant liberation of a hydrogen ion and of nicotinamide. They also showed that the reduced form of coenzyme 1 was not affected by the enzyme. These findings led to a formulation of the overall reaction as follows:

$$[\text{nicotinamide}^+\cdot\text{ribose-pyrophosphate-ribose-adenine}] + \text{HO}\cdot\text{H} \rightarrow \text{HO}\cdot\text{ribose-pyrophosphate-ribose-adenine} + \text{nicotinamide} + \text{H}^+ \quad (1)$$

where [nicotinamide$^+$·ribose-pyrophosphate-ribose-adenine] denotes coenzyme 1, and HO·ribose-pyrophosphate-ribose-adenine denotes the (ribose-pyrophosphate-ribose-adenine) derivative of coenzyme 1 after its nicotinamide moiety has been replaced by a hydroxyl-group.

Later, Zatman *et al.*[4] found that mammalian diphosphopyridine nucleotidase also catalyses an exchange reaction between free nicotinamide and the nicotinamide moiety of coenzyme 1. An explanation of this phenomenon was offered by Zatman *et al.*[4] by postulating a two-step reaction:

$$[\text{nicotinamide}^+\cdot\text{ribose-pyrophosphate-ribose-adenine}] + \text{enzyme} \rightleftharpoons [\text{enzyme}^+\cdot\text{ribose-pyrophosphate-ribose-adenine}] + \text{nicotinamide} \quad (2)$$

$$[\text{enzyme}^+\cdot\text{ribose-pyrophosphate-ribose-adenine}) + \text{HO}\cdot\text{H} \rightarrow \text{HO}\cdot\text{ribose-pyrophosphate-ribose-adenine} + \text{enzyme} + \text{H}^+ \quad (3)$$

Alivisatos *et al.*[5] found a diphosphopyridine nucleotidase in rabbit erythrocytes and described its distribution in these cells. They[6] also studied some of the requirements for the attachment of the substrate (coenzyme 1) on the enzyme. Later, Alivisatos and Woolley[7] solubilized and purified the diphosphopyridine nucleotidase from beef spleen, and, following a hypothesis of Woolley[8] on the utilization of the free energy of hydrolysis of 'onium' linkages, Alivisatos and Woolley[9] found that 5-amino-4-carboxamido-imidazole reacted with coenzyme 1 to form a new dinucleotide. In contrast to exchanges (for example, as in reaction 2), this imidazolytic[10] breakdown of coenzyme 1 was characterized by its irreversibility; the liberation of a hydrogen ion; and the presence of a trivalent nitrogen structure in the imidazole-ribose bond of the product[9]. The latter characteristic was most clearly demonstrated by the utilization of the new dinucleotide as a substrate in the enzymic formation of inosinic acid[10]. This demonstration established the identity of the imidazole-ribose bond in the dinucleotide with the imidazole-ribose bond present in the well-known precursor of purines, 5-amino-4-carboxamido-imidazole ribotide. Since the base-to-sugar configuration in coenzyme 1, in 5-amine-4-carboxamido-imidazole ribotide and in inosinic acid is the same (namely, β), the above-mentioned identity[10] implied a retention of configuration during the imidazolytic process and pointed towards a two-step reaction, each involving a Walden inversion[11]. The first step should be identical to the first step encountered in hydrolytic processes (reaction 2). This would also account for the inhibitory effect of nicotinamide upon the imidazolytic breakdown. The second step could be summarized in reaction (4), which should be taken as an alternative of reaction (3), if the imidazole is present in the medium:

[enzyme$^+$·ribose-pyrophosphate-ribose-adenine] + imidazole → enzyme + imidazole·ribose-pyrophosphate-ribose-adenine + H$^+$ (4)

where imidazole denotes the 5-amino-4-carboxamido-imidazole and other symbols have the same meaning as in reaction (1).

The finding[12] that another imidazole, namely, histamine, is even more capable of participating in reaction (4) focused new interest on the reactions catalysed by diphosphopyridine nucleotidase and called for a unified theory of action of this enzyme. (The "dinucleotide II" mentioned in a previous publication[12] proved later to be an artefact arising during the isolation procedures from "dinucleotide I". The imidazole-ribose bond of the latter has a trivalent nitrogen structure at *p*H 7·0, but it acquires a proton at lower *p*H values (*pK'* about 4·0).)

The above-mentioned observations, together with recent preliminary experimental evidence mentioned in a later part of the article, led to the formulation of the following hypothesis concerning the identity and the catalytic mechanism of the active group(s) of mammalian diphosphopyridine nucleotidases of the glycosidase type:

The two steps encountered in both the hydrolytic and imidazolytic processes (reactions (2), (3) and (4)) are virtually a succession of two nucleophilic attacks (each involving an inversion) upon carbon 1′ of the ribose moiety of coenzyme 1 close to nicotinamide. In the first (common) step the nucleophilic agent is a residue on the enzyme, while in the second step this part is played by water (hydrolysis) or an imidazole (imidazolysis).

While various groups of the diphosphopyridine nucleotidase may be important for its catalytic activity, our present evidence (see below) favours the participation of its histidyl-moieties. Of the possible forms of the amidine part of histidyl groups on the enzyme, the non-ionized form is expected to predominate over the *p*H range of activity of diphosphopyridine nucleotidases[6]. Certain contribution to the catalytic activity may possibly come from the anionic (deprotonated) form, especially at high *p*H values[13]. However, for clarity of discussion, only the non-ionized form is illustrated in Fig. 1 as participating in the catalysis. Thus, provided that the proper requirements for attachment of the substrate (coenzyme 1) on the enzyme surface are fulfilled[6], nicotinamide may be displaced from coenzyme I by a histidyl group of the enzyme (Fig. 1, *a*). The structures in brackets in Fig. 1 correspond to the [enzyme$^+$·ribose-pyrophosphate-ribose-adenine] intermediate encountered in reactions (2), (3) and (4).

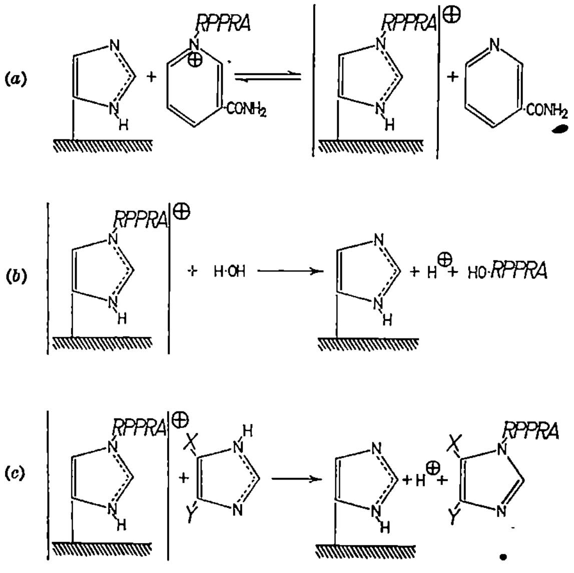

Fig. 1. Proposed scheme for the diphosphopyridine nucleotidase activities: *a*, exchange; *b*, hydrolysis; *c*, imidazolysis. The extreme (reactive) forms of histidyl groups of the free enzyme would be those of dipoles. *X* and *Y*, various radicals; RPPRA, ribose-pyrophosphate-ribose-adenine

In the absence of an excess of nicotinamide, other nucleophilic agents, for example, a hydroxyl or an imino-nitrogen of an imidazole, may react with the intermediate (Fig. 1, reactions *b* and *c*). The irreversibility of reactions *b* and *c* is due to the absence of an 'onium' structure in the products (HO·ribose-pyrophosphate-ribose-adenine and imidazole·ribose-pyrophosphate-ribose-adenine). An 'onium' structure like the one present in the oxidized form of coenzyme 1 (Fig. 1, reaction *a*) is necessary for the reversible exchange of the ·ribose-pyrophosphate-ribose-adenine radical with the enzyme. Thermodynamically, the necessity for a quaternary nitrogen structure reflects the higher free energy of hydrolysis of the nicotinamide-ribose bond, as compared with the free energy of hydrolysis of the imidazole-ribose bond[10].

A deeper understanding of the 'onium' structure requirement may be achieved by comparison with a simpler system, namely, the imidazole catalysis of hydrolysis of *p*-nitrophenyl-acetate[13,14]. In that case, a low electron density in the vicinity of the carbonyl-carbon atom (Fig. 2) is a major factor in determining the susceptibility of this carbon to a nucleophilic attack (for a discussion of other factors, see ref. 13). The nucleophilic agent is an imidazole, acting in a manner similar to the one postulated above for diphosphopyridine nucleotidase (Fig. 1). In the reaction catalysed by diphosphopyridine nucleotidase, on the other hand, the glycosidic carbon atom of a ribose moiety of coenzyme 1 is the target for the nucleophilic attack. This carbon is rendered to a certain extent electrophilic by the attached 'onium' structure (Fig. 2). While this polarization of the nicotinamide-ribose bond is apparently insufficient to make coenzyme 1 a suitable substrate for an

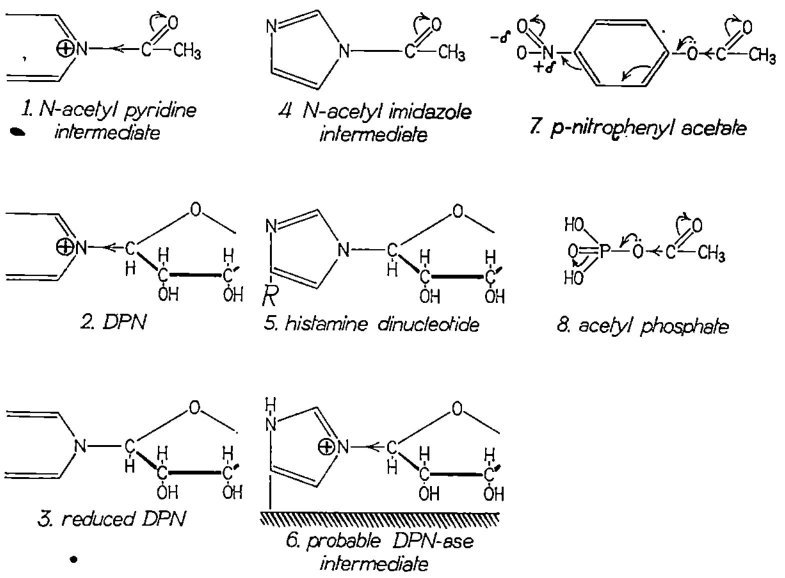
1. N-acetyl pyridine intermediate
2. DPN
3. reduced DPN
4. N-acetyl imidazole intermediate
5. histamine dinucleotide
6. probable DPN-ase intermediate
7. p-nitrophenyl acetate
8. acetyl phosphate

Fig. 2. Substrates, intermediates and end-products involved in reactions catalysed by pyridine, imidazole and diphosphopyridine nucleotidase

imidazole-catalysed hydrolysis[12], imidazolyl groups of the enzyme are probably capable of serving this purpose. A study of the influence of the various groups attached upon the carbon atom which serves as the electrophilic centre in substrates and intermediates (Fig. 2) involved in the hydrolytic processes catalysed by pyridine[11], imidazole[13,14] and the diphosphopyridine nucleotidase, will clarify this point better. Of the three substrates involved in these hydrolytic processes, namely, acetyl-phosphate, *p*-nitrophenyl-acetate and coenzyme 1 respectively, the latter is the most stable to spontaneous hydrolysis. This is due to the presence of a glycosidic structure, instead of a carbonyl, in the susceptible site of coenzyme 1. On the other hand, all three intermediates, namely, N-acetyl-pyridinium, N-acetyl-imidazole and the [enzyme$^+$·ribose - pyrophosphate-ribose-adenine], hydrolyse spontaneously after their formation. However, N-acetyl-pyridinium[11] has a much shorter life than N-acetyl-imidazole[14] in water. This is due to the presence of an 'onium' structure in the former intermediate[14]. The importance of an 'onium' structure in promoting the ability of such a bond to hydrolysis is further demonstrated by the well-known higher stability of the reduced form of coenzyme 1 to alkaline hydrolysis, as compared to its oxidized form (Fig. 2). The lability of the N(ring)-acetyl-histamine intermediate[13], as compared to the high stability of the imidazole-ribose bond in the histamine dinucleotide (Fig. 2), illustrates the importance of a carbonyl structure or other means tending to intensify the electrophilic character of the carbon atom at the site of the nucleophilic attack.

By analogy with the above examples, the extreme lability of the [enzyme$^+$·ribose-pyrophosphate-ribose-adenine] intermediate is probably due to a concerted action of an 'onium' structure and of other groups on the enzyme surface tending to increase the electrophilic character of the glycosidic carbon atom. The problem of the nature of the latter groups is left, at present, open.

The availability of soluble purified diphosphopyridine nucleotidase[7] prompted a more direct experimental approach to the problem of the identity of the active centre(s) of the enzyme. Although our evidence is as yet of a preliminary nature, it strongly favours the hypotheses put forward here. In each of these experiments 16 units of the enzyme (0·4 mgm. of protein) were treated, in a 5 per cent sodium bicarbonate medium (*p*H 8·0, 3·0 ml. total vol.), with the various reagents indicated in Table 1. When 2,4 : dinitrofluorobenzene was used, the reaction was carried in a heterogeneous system with 0·25 ml. of the reagent added. In this instance, the watery phase of both the experimental system and its control contained, in addition to bicarbonate, 5 per cent methanol. All other reagents were soluble, in the concentrations employed, in the bicarbonate medium. Proper controls (no reagent added) accompanied all experiments. The mixtures were shaken at a slow rate (prevention of frothing) at 4° C. for periods indicated in Table 1. At the end of the incubation, the samples were transferred in casings and dialysed, in separate containers, against 200 ml. of 5 per cent sodium bicarbonate, at 4° C. The apparatus allowed a continuous mixing of the contents of the casings as well as of the outside liquid in the containers. The latter was changed 4 times in a period of 48 hr. Hydrolytic diphosphopyridine nucleotidase activity was tested as previously[7].

As shown in Table 1, 2,4 : dinitrofluorobenzene completely abolished the enzymic activity of the sample. Photo-oxidation with methylene blue had the same effect. If —SH groups can be excluded on other grounds (see below), this effect of methylene blue is regarded as rather specific for the histidyl residues of a protein[15]. Fluorescein *iso*thiocyanate reacts primarily with free aliphatic amino-groups (for example, lysine). However, we found that it also reacts with imidazoles (for example, acetyl histamine). In accordance, it had an effect on the diphosphopyridine nucleotidase activity (Table 1). Azo-enzyme, prepared by reaction with 3·75 µmoles of diazotized sulphanilic acid, was completely inactive. However, a ten times smaller amount of the reagent resulted in only partial inactivation. These results indicate reaction first with tyrosyl residues and, afterwards, with histidyl groups of the protein. However, anomalies in the interaction of diazo-

Table 1. EFFECT OF VARIOUS REAGENTS UPON THE ACTIVITY OF DIPHOSPHOPYRIDINE NUCLEOTIDASE

Reagent	Total amount of reagent (µmol.)	Duration of reaction (hr.)	Per cent loss of hydrolytic activity
1. 2,4 : Dinitrofluorobenzene	excess	2	100
2. Methylene blue (light)	1·400	6	100
3. Methylene blue (darkness)	1·400	6	9
4. Fluorescein *iso*thiocyanate	2·500	2	25
5. Fluorescein *iso*thiocyanate	2·500	16	56
6. Diazotized sulphanilic acid	0·375	16	45
7. Diazotized sulphanilic acid	3·750	16	100
8. Iodine (in 0·1 *M* potassium iodide)	0·500	6	14
9. Iodine (in 0·1 *M* potassium iodide)	10·000	6	100
10. Iodoacetate	5·000	16	0
11. *p*-Chloromercuribenzoate	0·320	6	0
12. *p*-Chloromercuribenzoate	6·500	6	0

reagents with proteins should be kept in mind[16]. The effect of iodine (Table 1) may be interpreted in a similar manner. Iodoacetate and *p*-chloromercuribenzoate did not have any appreciable effect on the activity of diphosphopyridine nucleotidase. The exclusion of —SH groups as possible participants in the enzymic activity was rather unexpected, in view of results by Stadtman *et al.*[17]. These workers discovered an enzyme that catalyses a reaction between acetyl-S-coenzyme *A* and imidazole to form the N-acetyl derivative.

Histidyl residues have been regarded as essential to the activity of several hydrolytic enzymes (see refs. in 13 and 14). According to our experimental findings, this seems to be also true for the diphosphopyridine nucleotidase. Considering the diverse catalytic capacities of this enzyme (namely, exchanges, hydrolytic and imidazolytic processes), that essentially parallel the various model systems developed for the study of the mechanism of enzymic hydrolysis, diphosphopyridine nucleotidase may prove very useful for such studies.

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MOLECULAR ADAPTATION IN HÆMOGLOBINS: NATURE OF THE BOHR EFFECT

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SCHMIDT-NIELSEN[1] has shown that among terrestrial mammals the smaller the animal the higher is the oxygen pressure (P_{50}) at which the whole blood is half-saturated with oxygen. Thus the blood is adapted to deliver oxygen to the tissues at higher pressures in the smaller animals the specific rates of oxygen consumption of which are highest.

Recently, I have found[2] that the primary difference between these bloods lies in the sensitivity of their hæmoglobins to changes in *p*H. As the 'Bohr effect', it is well known that high carbon dioxide pressure or decreased *p*H tends to dissociate oxyhæmoglobin, and so promotes gas exchange in the tissues. In a series of terrestrial mammals, ranging in size from elephant to mouse, the smaller the animal the greater is the sensitivity of the oxygen equilibrium of its hæmoglobin to *p*H. This *p*H sensitivity (Bohr effect) reflects the fact that certain acid groups of the hæmoglobin are functionally linked to the oxygenation process in such a way that they become more acidic when oxygen is bound[3,4]. Therefore, the results indicate that the smaller the mammal the greater is the number of protons discharged from its hæmoglobin when the molecule is oxygenated. This effect not only promotes gas exchange but also is a homœostatic buffering mechanism.

I have now determined the number of mercuric ions which can be immediately bound to these hæmoglobins, using the amperometric procedure of Kolthoff, Stricks and Morren[5]. The hæmoglobin solutions were prepared as previously described[6]. The titrations were performed at 25° C. in an atmosphere of helium; thus reduced hæmoglobin was titrated. These titrations indicate a linear relation between the magnitude of the Bohr effect, defined as $\Delta \log P_{50}/\Delta p\mathrm{H}$, and the number of mercuric ions bound per molecule of hæmoglobin. This is shown in Fig. 1. Only the rabbit appears really exceptional.

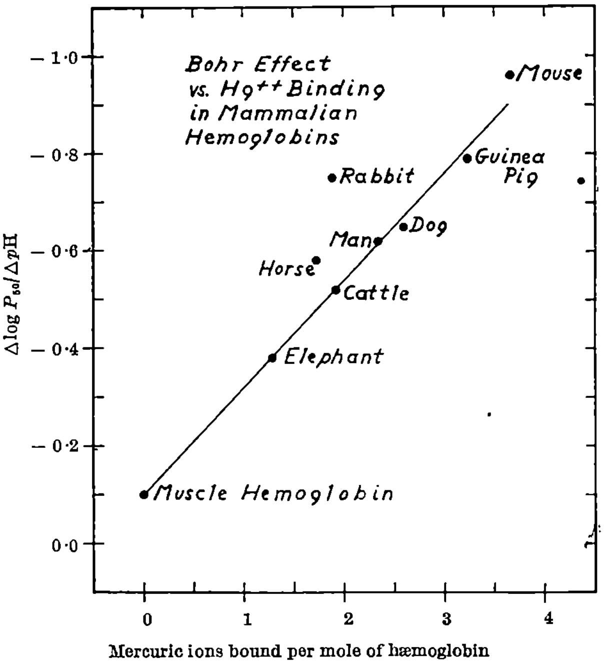

Fig. 1. The relation between the magnitude of the Bohr effect and the number of mercuric ions which can be bound per hæmoglobin molecule. The data for muscle hæmoglobin are from Theorell (ref. 8)

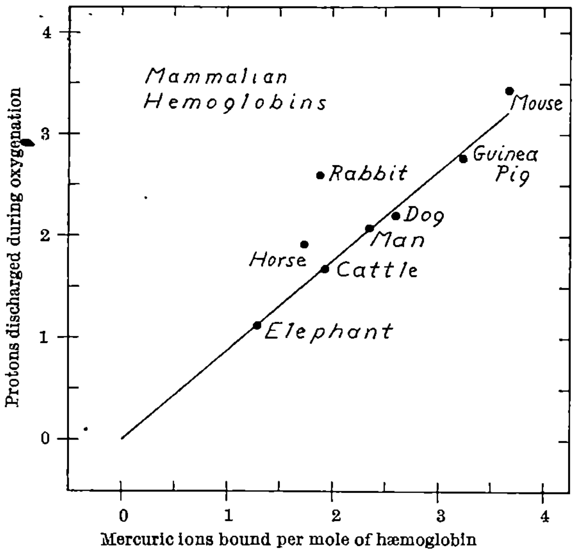

Fig. 2. The relation between the number of protons discharged by hæmoglobin during its oxygenation as calculated in the text, and the number of mercuric ions which may be bound per molecule

Thus the magnitude of the Bohr effect appears to be directly proportional to the number of sulphydryl groups.

The conclusion that the oxygen-linked acid groups are sulphydryl groups is strengthened by the following considerations. Horse-muscle hæmoglobin has no sulphydryl groups[7]; the value of its Bohr effect[8] is approximately 0·1. Extrapolation of the line in Fig. 1 to the point at which zero mercuric ions are bound corresponds to just this value. If we assume that the small non-sulphydryl Bohr effect exhibited by muscle hæmoglobin is also present in all the blood hæmoglobins, then we can subtract the Bohr effect value in muscle hæmoglobin from all the other values to obtain the Bohr effect due solely to sulphydryl groups. Wyman has shown that $\Delta\log P_{50}/\Delta p\mathrm{H}$ is directly proportional to the number of protons discharged during oxygenation[4]. Therefore we should be able to calculate the number of sulphydryl protons dissociated during oxygenation. In Fig. 2 the number of protons so calculated is plotted against the number of mercuric ions bound. It is clear that a rather good one-to-one quantitative correspondence exists. The number of mercuric ions bound is only 10 per cent higher than the number of protons dissociated. If the oxygen-linked acid groups are sulphydryl groups, the binding of these groups with an irreversible reagent such as N-ethyl maleimide should result in greatly reducing the magnitude of the Bohr effect. We find that low concentrations (5 moles N-ethyl maleimide per mole of hæmoglobin) have just this effect: not only is the oxygen affinity increased but also the magnitude of the Bohr effect decreases greatly: $\Delta\log P_{50}/\Delta p\mathrm{H}$ drops from 0·65 to 0·28 in human hæmoglobin at 35° C.

These observations led us to predict that whenever we find hæmoglobins the oxygen equilibria of which are insensitive to *p*H (no Bohr effect), we might expect to find either no, or a very small number of, sulphydryl groups. I had previously found that tadpole hæmoglobin has no Bohr effect whereas that of the adult bullfrog has a large Bohr effect[5]. I have re-examined tadpole hæmoglobin, and find that it binds the smallest number of mercuric ions of any blood hæmoglobin so far examined: only 0·8 mercuric ion per mole of hæmoglobin. In contrast, the adult bullfrog hæmoglobin molecule binds about 4·2 mercuric ions.

It is well known that the four hæm groups present in each hæmoglobin molecule interact with one another. That is, oxygenation of certain of these hæms greatly enhances the affinity of other hæms for oxygen. I have shown previously that sulphydryl reagents can abolish this interaction[6–10]. It now appears that the interaction is destroyed when mercurials are bound to the oxygen-linked acid groups which are now identified as sulphydryl groups. Thus two properties of hæmoglobin of great physiological importance, the S-shape of the oxygen equilibrium curve and the dependence of the equilibrium on *p*H, are both mediated by sulphydryl groups.

The suggestion that the oxygen-linked acid groups are imidazole residues was based on the correspondence between the observed *pK* values and heats of dissociation and those of imidazole[4], and on the changes anticipated in the electronic structure of imidazole resulting from covalent linkage with the hæm iron[11]. Unfortunately, both the *pK* values and the heats of dissociation are often very similar in both —SH groups and imidazole[12,13]. Although mercurials do have affinity for imidazole groups, the affinity for —SH groups is generally much higher. Furthermore, in human hæmoglobin at least, a one-to-one correspondence exists between the number of N-ethyl maleimide molecules bound, and the number of cysteine residues found analytically[14]. In our experiments the number of mercuric ions that can be immediately bound by human hæmoglobin drops by two-thirds within 5 min. after the addition of five moles of N-ethyl-maleimide per mole of hæmoglobin; the mercury titration is zero after 15 min. The effect of N-ethyl-maleimide on the oxygen equilibrium is very similar to that of the mercurial, mersalyl.

These observations suggest that one of the primary physiological adaptations of hæmoglobins is brought about by varying the number of cysteine residues per molecule. If it is physiologically advantageous for an animal to possess a hæmoglobin with a large Bohr effect, mutants with hæmoglobins possessing a larger number of appropriately placed cysteine residues would be selected. This conclusion is supported by the amino-acid analyses of Birkofer and Taurins[15], who examined the hæmoglobins of 7 species of mammal. Their results clearly indicate an inverse relation between body-weight and number of cysteine residues in each hæmoglobin.

A full report of these experiments will be published elsewhere. I wish to acknowledge the assistance of Messrs. Patrick Barlow and Allen Tyler. The research was supported in part by a grant from the National Science Foundation.

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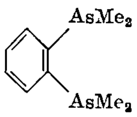
LETTERS TO THE EDITORS

CHEMISTRY

New Oxidation States of Technetium

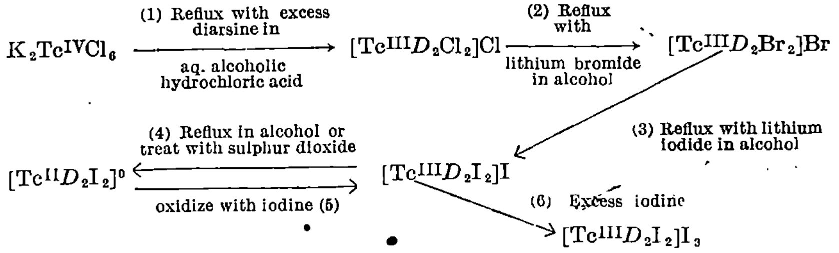
THE chemistry of technetium, the middle member of the Group VII triad with manganese and rhenium as its congeners, has been little investigated until recently owing to its rarity. Indeed, since the isolation of the isotope technetium-99 in gram quantities from the products of uranium fission[1] the oxidation states +7 and +4 only have been definitely established for this element, at least in solid compounds. These are exemplified by $KTcO_4$ and Tc_2S_7 in the first case and TcO_2, TcS_2, $TcCl_4$ and K_2TcHal_6 (Hal = Cl, Br and I) in the second[1]. Evidence[2] for the existence of green tervalent technetium in solution has been adduced from the reducing power of an electrolytically produced aqueous solution, but no compound of technetium III was isolated. Similarly, technetium V probably exists in solution as the complex thiocyanate, but no solid compound has been isolated[3]. The close similarity of rhenium and technetium suggested that for the preparation of lower oxidation states of technetium a study of the corresponding rhenium chemistry would be very helpful.



Ditertiary arsine (*D*)

Recent work[4] has shown that very stable bivalent and tervalent rhenium compounds may be prepared by using the ditertiary arsine (*D*) as a chelating ligand. These have the general formula $[Re^{II}D_2X_2]^0$ and $[Re^{III}D_2X_2]ClO_4$, where X = Cl, Br or I. The bivalent complexes are non-electrolytes, paramagnetic, ($\mu \approx 1{\cdot}8$–$1{\cdot}9$ Bohr magnetons) and are clearly octahedral, spin-paired d_ε^5 compounds. The tervalent derivatives are uni-univalent electrolytes in nitromethane and clearly involve octahedrally co-ordinated rhenium III with a d_ε^4 configuration. The magnetic moments ($\approx 1{\cdot}9$ Bohr magnetons) are less than the spin-only value for two unpaired electrons (2·83 Bohr magnetons), but these are readily understood in terms of the Kotani[5] theory for octahedral strong-field complexes of elements with a large spin-orbit coupling constant.

Following the procedure used to obtain the above rhenium compounds, we have now been able to prepare the corresponding technetium II and technetium III derivatives. Starting from potassium hexachlorotechnetate[6], the sequence of reactions employed is as follows :


K₂TcIVCl₆
(1) Reflux with excess diarsine in
aq. alcoholic hydrochloric acid
[TcIIID₂Cl₂]Cl
(2) Reflux with
lithium bromide in alcohol
[TcIIID₂Br₂]Br
(3) Reflux with lithium iodide in alcohol
[TcIIID₂I₂]I
(4) Reflux in alcohol or treat with sulphur dioxide
[TcIID₂I₂]⁰
oxidize with iodine (5)
(6) Excess iodine
[TcIIID₂I₂]I₃

Having only 15 mgm. of technetium, the usual analytical procedures are not feasible, but reactions 2 and 3 have been confirmed quantitatively by measuring both the amount of the less electronegative halide entering the complex and the amount of more electronegative halide which is displaced. Reaction 5 has been shown to proceed with the uptake of exactly one equivalent of iodine. Conductivity, molecular weight and magnetic data have been obtained on these compounds and, taken in conjunction with the known properties of the corresponding Re II and III derivatives, provide further confirmation of the composition and structure of the new complexes. Finally, it has been shown by X-ray powder photographs that the rhenium II and technetium II compounds are isomorphous. The properties of these compounds are summarized in Table 1.

Table 1. COMPOUNDS OF TECHNETIUM III and II

Oxidation state	Compound	Colour	$\mu_{eff.}$ (20°) B.M.	Spectra λ mμ	$\varepsilon \times 10^{-3}$	Molecular conductivity in nitromethane 25° C. $C = 1 \times 10^{-3} M$*
Tc^{III} (d^4)	$[TcD_2Cl_2]Cl$	Orange	2·7	441	3·92	75 ohm^{-1}
	$[TcD_2Br_2]Br$†	Red	3·2	472 302	5·56 3·08	77 ohm^{-1}
	$[TcD_2I_2]I_3$	Deep red to black	3·4	574 359 294	4·00 6·69 11·23	86 ohm^{-1}
Tc^{II} (d^5)	$[TcD_2I_2]^0$‡	Brown	~3·0	514 474	2·79 1·00	Slightly soluble but a non-electrolyte in $Ph NO_2$ and nitromethane

* Λ_M for a uni-univalent electrolyte in nitromethane at 10^{-3} *M* is 70–90 ohm^{-1}.

† Molecular weight. Found 435, isopiestic in acetone. Calculated for 1 – 1 electrolyte 455.

‡ From X-ray powder photographs the $[TcD_2I_2]^0$ is isomorphous with $[ReD_2I_2]^0$, and $[TcD_2I_2]I_3$ with $[ReD_2I_2]I_3$.

The tervalent technetium compounds are similar to those of tervalent rhenium, except that the magnetic moments are higher, as expected. They differ very much from the known[7] diarsine complexes of manganese III, which are spin-free and have the general formula $[MnDX_2.H_2O]ClO_4$, where X = Cl or Br.

Bivalent technetium resembles both manganese II and rhenium II in forming compounds of the type $[Tc^{II}D_2I_2]^0$, but the magnetic moment of this compound is unusual, agreeing neither with the spin-free value for five unpaired electrons as in $[MnD_2I_2]^0$, nor with the spin-paired value for one unpaired electron as in $[ReD_2I_2]^0$. The position of technetium in the periodic table provides a clue to this behaviour which will be discussed in a more detailed report on these compounds to be published shortly.

We are grateful to the United Kingdom Atomic Energy Authority for the loan of the technetium used in this work. One of us (J. E. F.) also thanks the University of New Zealand for a postgraduate scholarship.

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Cyclic Alternating-Current Voltammetry with a Platinum Electrode

The a.c. polarographic method of Brewer and Gutmann[1], in which a.c. instead of d.c. current is measured against polarization potential, has hitherto not been extended to the determination of compounds reducible or oxidizable at potentials more positive than the potential of dissolution of mercury. This limitation is due to the difficulty of reproducing a.c. current-voltage curves obtained with solid electrodes. Changes in the nature of the surface of the electrode are responsible for poor reproducibility in conventional voltammetry[2]; even worse results can be expected in a.c. voltammetry because changes in the nature of the electrode modify the impedance much more than the resistance of the double layer during the electrolytic process.

One can expect an electrode to acquire different reproducible states of accommodation during the electrolytic processes when submitted to a series of cyclic polarizations in a solution to be investigated. Kemula and Kublick[3] (and Kemula, K., personal communication) have already shown that perfectly repeatable d.c. polarograms are obtained when a hanging-drop mercury electrode is polarized cyclicly at a moderate rate between 0·2 and − 2·0 V. versus a standard calomel electrode. In fact, reproducible a.c. polarograms are also recorded with a platinum electrode when the electrode is polarized cyclicly at approximately 2·5 V./min. between − 1·0 and 1·5 V. versus a standard calomel electrode in a solution through which nitrogen is bubbling.

Besides their perfect repeatability, cyclic a.c. polarograms obtained with a platinum electrode have two important properties: (1) with alternating current most of the characteristic peaks appear only on the portion of the polarogram scanned from negative to positive, the portion of the cycle scanned in the opposite direction to that normally used; (2) the position and the height of the characteristic peaks are practically unaffected by the mechanical stirring of the solution.

As an example, Fig. 1 shows two recorded cyclic polarograms (curves 1 and 2) of 0·1 *M* sodium perchlorate solutions containing $2 \cdot 5 \times 10^{-6}$ *M* and 5×10^{-4} *M*, respectively, of potassium iodide, together with their d.c. polarograms (curves 1′ and 2′). These polarograms were obtained with a 3 $mm.^2$ platinum/10 per cent rhodium wire working electrode and a 25 $cm.^2$ saturated calomel auxiliary electrode. The a.c. polarograms were obtained by feeding the cell with a 60 c./s., 0·03 root mean square sinusoidal voltage, in parallel with the linearly scanned d.c. voltage. The a.c. and d.c. currents were restricted from other circuits by a low-resistance 10-henry inductor and by a capacitor of a few microfarads placed in the d.c. and a.c. circuits, respectively. The relative admittance of the cell is determined by the voltage drop across a resistor located in the a.c. circuit. This voltage was measured in these experiments with an electronic a.c. millivoltmeter, and was recorded through a self-balancing millivolt potentiometer.

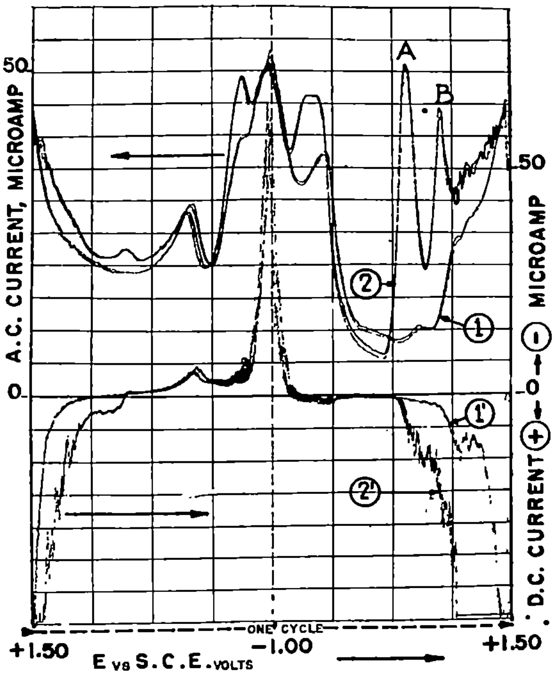

Fig. 1. Cyclic a.c. (curves 1 and 2) and d.c. (curves 1′ and 2′) polarograms of 0·1 *M* sodium perchlorate solution containing potassium iodide: (*a*) $2 \cdot 5 \times 10^{-6}$ *M* (curves 1 and 1′); (*b*) $5 \cdot 0 \times 10^{-4}$ *M* (curves 2 and 2′)

The addition of 0·5 m*M* potassium iodide to the 0·1 *M* sodium perchlorate solution (curves 2 and 2′) markedly affected the shape of the second half-cycle of the a.c. polarogram, while the shape of the part scanned from positive to negative of the curve remained practically unchanged. The repeatability of the curve is so good that there is scarcely any difference between the duplicated curves recorded in Fig. 1 despite the complicated pattern of the curve. No clear relation appeared between the admittance peaks *A* and *B* of the 0·5 m*M* potassium iodide solution and the cyclic d.c. polarogram of the same solution (curve 2′). The diffusion current of the d.c. polarogram showed irregular fluctuations due to the nitrogen bubbling. No such fluctuations appear on the a.c. polarogram.

The height of peaks *A* and *B* increases with the concentration of iodide, and seems to be determined by the rate of oxidation of iodide ions adsorbed on the electrode. The height of peak *B*, which increases with the addition of iodine and decreases with the addition of starch or thiosulphate, seems to be related to the rate of oxidation of adsorbed iodine, probably to I^+. The amount of iodide and iodine contained in the solution can be determined by the height of the peaks *A* and *B* after establishment of a calibration curve.

Perfectly repeatable cyclic a.c. polarograms are also obtained when compounds like ferricyanide or hydroquinone, which are reversibly or semi-reversibly reducible or oxidizable between the potential of evolution of hydrogen and oxygen, are added to a sodium perchlorate solution. Repeatable polarograms are obtained even with species like Ag^+ and Pb^{2+}, which form a deposit on the surface of the electrode, when the solution is made acid with perchloric acid. In this case the results are repeatable so long as the amount of product reduced during the first half-cycle is still completely re-oxidized during the next one. The peak maximum obtained with deposited metal coincides quite well with the moment at which the last trace of the reduced product disappears at the surface of the electrode.

Cyclic a.c. voltammetry with a platinum electrode can therefore be used as a convenient method for the analysis of compounds reversibly or semi-reversibly reducible or oxidizable at potentials between $-1{\cdot}0$ and $+1{\cdot}5$ V. versus a standard calomel electrode. It also appears to be an excellent method for studying the mechanism of electrolytic processes at a solid electrode.

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Polymorphic Conversion of Mercuric Iodide on Alumina

It is well known that mercuric iodide exists in two crystalline forms, the stable red form being converted to the metastable yellow at 127° C.[1]. Recently, Sieskind[2] has reported an orange modification which was isolated from both ethyl acetate and acetone.

The information available concerning the spectral characteristics of mercuric iodide in solution is apparently limited to a paper by Gewenlock and Trotman[3], who have reported that the transmission spectrum of red mercuric iodide in ethanol has two broad absorption bands in the ultra-violet, with maxima at approximately 215 and 273 mμ. No mention is made of any characterizing absorption in the visible region. There are no comparable results regarding the metastable yellow form which quickly reverts to the red form upon standing or treatment with solvents.

Work by Zeitlin and Niimoto[4] showing that characteristic reflexion spectra of solids could be obtained on active adsorbents provided a method for the measurement of the spectra of both the red and the yellow forms in the solid state.

A small quantity (50 mgm.) of powdered red mercuric iodide of analytical grade was mixed with 2·5 gm. of active chromatographic alumina (>140 mesh) Woelm—activity grade 1. Within a short time it became evident that a conversion from the red to the yellow form was occurring. The change from a heterogeneously dispersed mixture of red mercuric iodide and alumina to one which was decidedly yellow and homogeneous in appearance was striking and practically complete in a few days at room temperature. The transition proceeded at 0° C. but at a much slower rate. It was substantially accelerated by mild heating. Although the yellow form is unstable when prepared in the usual manner, it apparently can be stabilized and maintained indefinitely on alumina in a moisture-free atmosphere. Exposure to the atmosphere or addition of water to the yellow form on alumina resulted in reversion to the red form. When the yellow form on alumina was extracted with ethanol or ether, the red modification was obtained.

The reflexion spectra of the solid mixtures were obtained with a Beckman *DU* spectrophotometer equipped with a standard reflectance attachment. Fig. 1, curves *a*, *b*, *c*, gives the spectra on alumina of the red, mixture of the red-yellow, and the yellow forms. The spectra, which are reproducible, differ in several details from the transmission spectra in ethanol. In reflectance, the first broad band is resolved into two smaller ones while the second maximum is retained. There is a definite bathochromic displacement of the optical peaks in going from transmittance to reflectance. In addition, there is a shoulder in the reflexion spectrum of the red form in the visible region which has not been reported in the transmission spectrum. In order to detect the spectral differences between the two forms, the spectra of the mixtures of mercuric iodide and alumina were taken immediately after mixing, after a few hours to permit partial conversion to the yellow modification, and after several days when the conversion to yellow mercuric iodide was complete. This enabled direct comparison of the spectra of the mixtures with identical quantities of mercuric iodide. The results show (Fig. 1, curves *a*, *b*, *c*), with increasing concentration of the yellow relative to the red form, a corresponding decrease in the absorbance in the shoulder region (about 560 mμ). The red form possesses in reflectance a shoulder in the visible that is absent in the yellow modification. It has been impossible to obtain the spectrum of the pure red form on alumina due to the change that takes place immediately after mixing. Consequently, red mercuric

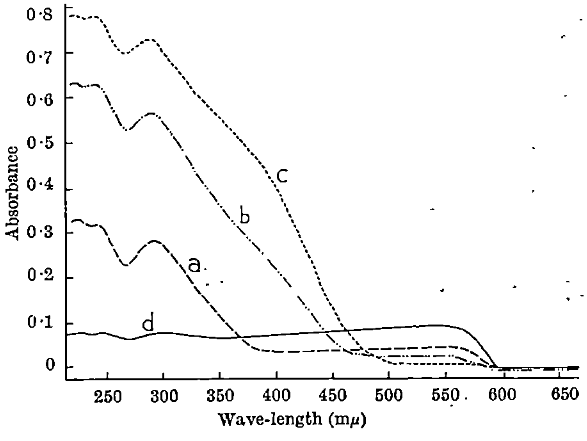

Fig. 1. Comparison of the reflexion spectra of polymorphic forms of mercuric iodide: *a*, red mercuric iodide on alumina; *b*, red-yellow mercuric iodide on alumina; *c*, yellow mercuric iodide on alumina; *d*, red mercuric iodide on sodium fluoride

iodide was mixed with powdered inactive sodium fluoride and the reflexion spectrum measured. The spectrum of pure red mercuric iodide (Fig. 1, curve *d*) so obtained is similar to the spectrum of the red form on alumina in all important details. The reflexion spectra of mercuric iodide on alumina are therefore not modified significantly by the active adsorbent.

Energy required for the conversion of the stable to the metastable form is apparently derived from the heat liberated by the adsorption of mercuric iodide on alumina. Our experimental findings are in agreement with the theory advanced by Tovbin and Baram[5] concerning the catalytic conversion of a stable to a less-stable form through heat of adsorption.

We gratefully acknowledge the financial support of the Research Corporation of New York provided by a Frederick Gardner Cottrell grant.

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Solution of Iodine in Phosphorus(III) *Isocyanate*

DURING an investigation of the solvent properties of phosphorus(III) *iso*cyanate[1] it was observed that iodine dissolved to give a reddish-brown solution. It is well known that such coloured solutions of iodine in 'active' solvents indicate some sort of solvent-solute interaction[2].

Previously[3], it had been noted that iodine dissolved in phosphorus trichloride to give a violet solution with an absorption maximum at 5000–5200 A. Since —NCO can be looked upon as a pseudo-halide, it might be expected that phosphorus *iso*cyanate and phosphorus trichloride would behave similarly in so far as reaction with iodine is concerned.

Iodine dissolves slowly in phosphorus *iso*cyanate with little heat of solution. The resulting solution is red-brown and shows an absorption maximum at 3300 A. If an excess of iodine is added to phosphorus *iso*cyanate a solid results. Removal of unreacted iodine with carbon tetrachloride yields an orange powder containing one half mole of iodine per mole of phosphorus *iso*cyanate. This adduct reacts violently with water, a property commonly associated with the species phosphorus(III). In contrast, chlorine reacts vigorously with phosphorus *iso*cyanate, sufficient heat being generated to boil the solution. The resulting yellow oil solidifies on contact with carbon tetrachloride to give a yellow crystalline solid, presumably $P(NCO)_3Cl_2$. The latter shows no evidence of phosphorus(III) formation after hydrolysis in water, thus indicating pentavalent phosphorus with chlorine bonded to phosphorus.

The colour of the solutions of iodine in phosphorus trichloride and in phosphorus *iso*cyanate may be a result of the inability of iodine to co-ordinate to phosphorus in the former (due to the electron-withdrawing power of chlorine) and the enhanced co-ordination in the latter (due to the electron donation of *iso*cyanate). Steric effects may also be involved in the case of iodine and phosphorus trichloride since no PCl_3I_2 has been confirmed, although such a compound has been reported[4].

The adducts $P(NCO_3)I$, as observed in this work, and PCl_3I [4] are similar in stoichiometry and would seem worthy of further investigation.

We wish to thank the Research Corporation of New York for financial support of part of this work.

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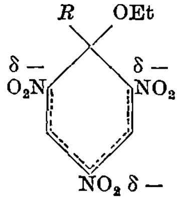
Interaction of 1,3,5-Trinitrobenzene with Ethoxide Ion

WHEN a dilute solution of 1,3,5-trinitrobenzene in ethanol is treated with sodium ethoxide, a yellow solution is formed. A similar colour is produced when sodium ethoxide is added to 2,4,6-trinitroanisole. The rates of development of the colours have been studied by Ainscough and Caldin[1], who found that there are two colour-producing reactions : (i) a 'fast' reaction the product of which they suggest is a charge-transfer complex, and (ii) a 'slow' reaction, which probably produces an addition compound where OEt is covalently bonded to the nucleus, as was suggested by Meisenheimer[2] for the solid obtained in this reaction (I, R = OCH_3). With 1,3,5,-trinitrobenzene and sodium ethoxide only one reaction was observed, and on the basis of similar rates of reaction and similar effects of acid on the two systems, Ainscough and Caldin suggested that the product is a charge-transfer complex analogous to the 'fast' reaction with 2,4,6-trinitroanisole. The absorption spectra of the trinitrobenzene + sodium ethoxide obtained by them did not resemble that of trinitroanisole + sodium ethoxide.



(I)

The absorption spectrum of 2,4,6-trinitroanisole in ethanol in the visible region in the presence of an excess of potassium ethoxide has been re-measured and compared with that of 1,3,5-trinitrobenzene under the same conditions. If measured within an hour of mixing at room temperature, the two spectra, expressed in terms of the formal molar extinction coefficient (optical density/molarity of nitrocompound) do resemble one another closely. Both solutions obey Beer's law and both bear a close resemblance to Meisenheimer's compound in acetone[3]. After a day, the spectrum of 1,3,5-trinitrobenzene in excess potassium ethoxide resembles that obtained by Ainscough and Caldin. Similar results were obtained using sodium ethoxide. This suggests that 1,3,5-tri-

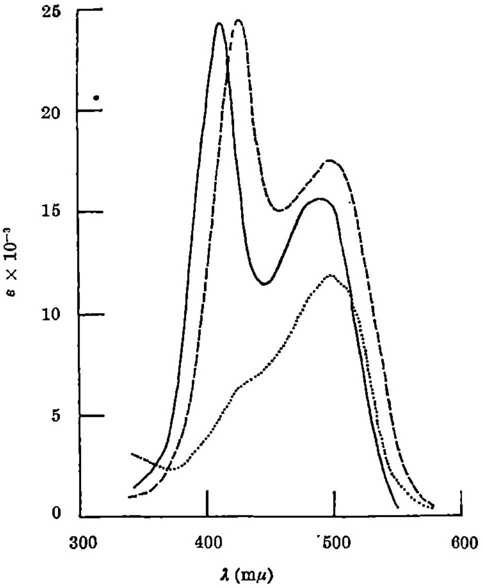


Fig. 1. ——, Potassium ethyl 1-methoxypicrate ($2{\cdot}27 \times 10^{-5}$ *M*) and potassium ethoxide ($6{\cdot}8 \times 10^{-2}$ *M*); – – – –, 1,3,5-trinitrobenzene ($3{\cdot}23 \times 10^{-5}$ *M*) and potassium ethoxide ($6{\cdot}8 \times 10^{-2}$ *M*) within 30 min. of mixing; . . . . , the same after 24 hr. All solutions in ethanol at 20° C.

nitrobenzene + ethoxide initially gives an addition product (I, R = H) which corresponds with the Meisenheimer compound.

The spectra were measured on an Optica *CF*4 grating spectrophotometer.

This work was carried out during the tenure of an Edward A. Deeds Fellowship of the University of St. Andrews.

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Relation between the Polarizability of Ions and other Significant Properties

In a previous communication[1] it was reported that the polarizability α of an ion is proportional to N^2 (N being the atomic number of the element). In order to examine the extent to which this relation, $\alpha = kN^2$, where k is a constant, is applicable in the case of ions, the data for the polarizabilities of ions[2] were plotted against the values of N^2 for the corresponding ions. It was found that it is applicable for elements in the same sub-group of the periodic table, although the proportionality constant k in this relation for earlier members of each sub-group differs from that applicable to the higher members of the same sub-group.

By applying this criterion, the element fluorine is found to differ from the other halogens, chlorine, bromine and iodine, in having a lower polarizability than that to be expected from the above formula. Similarly, lithium and sodium ions differ from potassium, rubidium and cæsium ions in group 1*A*, beryllium and magnesium differ from calcium, strontium, and barium ions, and so on. Such differences in the behaviour of the earlier elements in the sub-groups from those occurring higher up are in agreement with the corresponding differences in the chemical behaviour between fluorine on one hand and chlorine, bromine and iodine on the other, lithium and sodium from potassium, rubidium and cæsium and so on. This is evidently to be attributed to the electronic configurations in the atoms.

It is found also that for elements belonging to the same series in the different periods, the values of α decrease with increase in N^2.

Another interesting correlation has been obtained by plotting the values of the electric polarizabilities of ions against their magnetic susceptibilities, χ (see ref. 2). The graph thus obtained shows a distinct proportionality between the two, the relation being $\alpha = K_0\,\chi$, where K_0, the constant of proportionality, is different for positive and negative ions.

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PHYSICS

Nuclear Magnetic Resonance in Rolled Copper Sheet

An investigation has been made of the copper-63 nuclear magnetic resonance in rolled copper sheet. The specimens were made from an electrolytic copper of commercial purity and consisted of a pile of 18 sheets each measuring 0·6 cm. × 0·5 cm. × 0·0045 cm. and insulated from each other by rice paper of thickness 0·003 cm. The measurements were made with a Colpitts marginal oscillator at a frequency of 5·5 Mc./s., using a permanent magnet with pole pieces of 4·5 in. diameter and 1·5 in. gap.

The following features were observed.

(1) In sheet which has been recrystallized after heavy deformation by rolling (90 per cent reduction in thickness or more) the width of the line varies with the orientation of the specimen relative to the main magnetic field. This effect occurs for all annealing temperatures investigated (240–600° C.) but is more pronounced for the higher temperatures. If the specimen is rotated about the transverse direction (the direction in the plane of the sheet perpendicular to the rolling direction) the line-width shows minima for $\theta = 0$ and $\theta = \pi/2$, and a maximum for $\theta = \pi/4$, where θ is the angle between the main magnetic field and the plane of the sheet. The magnitude of the variation may be as much as ± 15 per cent in the mean square line-width.

This effect can be explained by the Van Vleck theory of dipolar broadening[1] if it is assumed that there is present in the specimen a preferred orientation of the type usually observed in recrystallized rolled sheet[2].

A variation of line-width with θ is also found for the deformed sheet; this is of a different nature from that in the annealed sheet, and is more difficult to interpret in terms of the expected preferred orientations.

(2) Annealing of a deformed specimen produces no detectable change in the shape of the resonance line, nor in its width except in the case of the most heavily deformed specimens (90 per cent reduction in thick-

ness). With these last specimens at all values of θ, except those near $\theta = \pi/4$, there is a narrowing of the line on annealing which is ascribed to a change in the preferred orientation; for $\theta = \pi/4$ there is no measurable change in the width. However, annealing causes an increase in the intensity of the line by about 25 per cent above that of the deformed sheet, and this increase appears to be independent of the degree of deformation in the range 25 per cent to 90 per cent reduction in thickness by rolling.

(3) For specimens of deformed sheet given a succession of heat treatments at temperatures increasing in steps of 10° C., the increase in intensity of the line is found to have taken place during treatments in a range of about 40° C., the variation being qualitatively similar to the variation in other properties of copper known to accompany recrystallization. The ranges of temperature are 200–240° C. for 90 per cent reduction and 230–270° C. for 50 per cent reduction. There is no apparent change in the shape of the line at any stage.

It has been reported by Bloembergen and Rowland[3] that the intensity of the absorption line in filed copper increases on annealing by a factor of up to 2, and this is ascribed to the non-appearance of the 'satellite' components of the line in the deformed material because of quadrupole interaction between the nucleus and the electric field gradients produced by dislocations. A similar explanation seems to be difficult to apply in the present case because of the absence of any marked broadening of the line: the observed increase would imply that in the deformed material about one-third of the nuclei are lying in a field gradient large enough to render the satellite components of their nuclear resonance unobservable, while the remaining two-thirds of the nuclei have their resonance virtually unaffected. Such an interpretation seems to imply either a discontinuous distribution of strain in the specimen, or a non-linear relation between strain and quadrupolar interaction energy. The discontinuities in strain which occur in the immediate neighbourhood of a dislocation line are not sufficient to explain the effect, since even if the dislocation density in the deformed material is as high as 10^{11} lines/cm.^{2}, only about 1 per cent of the atoms will lie within 5 interatomic distances of a dislocation line.

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Movement of Auroral Echoes and the Magnetic Disturbance Current System

A NUMBER of workers have reported systematic movement of very high-frequency radar echoes associated with auroral ionization. Bullough and Kaiser[1] at Jodrell Bank in England interpreted their results as indicating a westward movement before 2100 hr. local time and eastward thereafter. Unwin[2] at Invercargill in New Zealand, with an aerial directed 20° east of geomagnetic south, recorded radial motions which were northward before about 2230 hr. local time on the average, and southward thereafter. These results are consistent with those of Bullough and Kaiser. Recently, Nichols[3] in Alaska has recorded Doppler shifts with two aerials directed 30° each side of geomagnetic north, from which it was possible to determine an absolute direction and velocity. On most occasions the major component was in an east–west direction. Bullough *et al.*[4] at Jodrell Bank and Gadsden[5] at Invercargill have found a very good correlation between the occurrence of echoes and local magnetic activity. Further, Kaiser[6] found a good correlation between the mean component of radial velocity of echoes (in a direction 50° west of geomagnetic north) and the mean vertical component of the magnetic disturbance vector at Eskdalemuir for the days on which echoes were observed at Jodrell Bank.

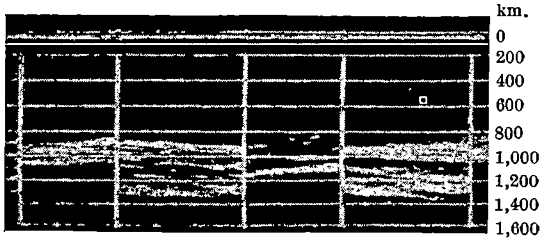

Fig. 1. Range – time record with antenna beam alternately oriented on 175° (for 6 min.) and on 240° (for 4 min.). Time increases from left to right

From this type of evidence it has been suggested by both Bullough *et al.*[4] and Nichols[3] that the movements observed are probably those of the electrons in the magnetic disturbance current system as deduced by Vestine *et al.*[7] from magnetic observations. Nichols calculated a current density of 10^3 amp./km. of latitude, which is of the same order as that deduced from magnetic observations in the auroral zone. The present communication gives further evidence that the movements of echoes can be identified with the disturbance current system, and shows that there is rough quantitative agreement between the two phenomena.

Since May 1958, the radar at Invercargill operating at 55 Mc./s. has been arranged so that the centre of the antenna beam is oriented alternately on geographical bearings of 175° (for 6 min.) and 240° (for 4 min.). The orientations have been chosen to avoid a region of low probability of echoes centred at 210° approximately[8]. An example of a range–time record obtained with this programme is shown in Fig. 1. Consistent radial velocities in each direction are apparent over a period of 20 min., and it is justifiable to calculate an absolute velocity and direction from the radial components read from each consecutive pair of records. In the preliminary calculations no corrections have been made for the fact that the geographical direction of the radar beam varies slightly with range owing to the curvature of the Earth. This change is quite negligible at a bearing of 175°. At 240° it amounts to 10° at 1,200 km., which is small compared with the radar beam-width of 25°.

A histogram of all absolute directions observed between May and August is shown in Fig. 2*a*. They have been calculated separately for the range-intervals 0–400 km., 400–800 km. and 800–1,200 km. from the radar, but there is no systematic change in direction with range. The bulk of the directions measured are close to local magnetic east–west. On any one occasion the change from westerly to easterly movement during the night is quite distinct, though it may

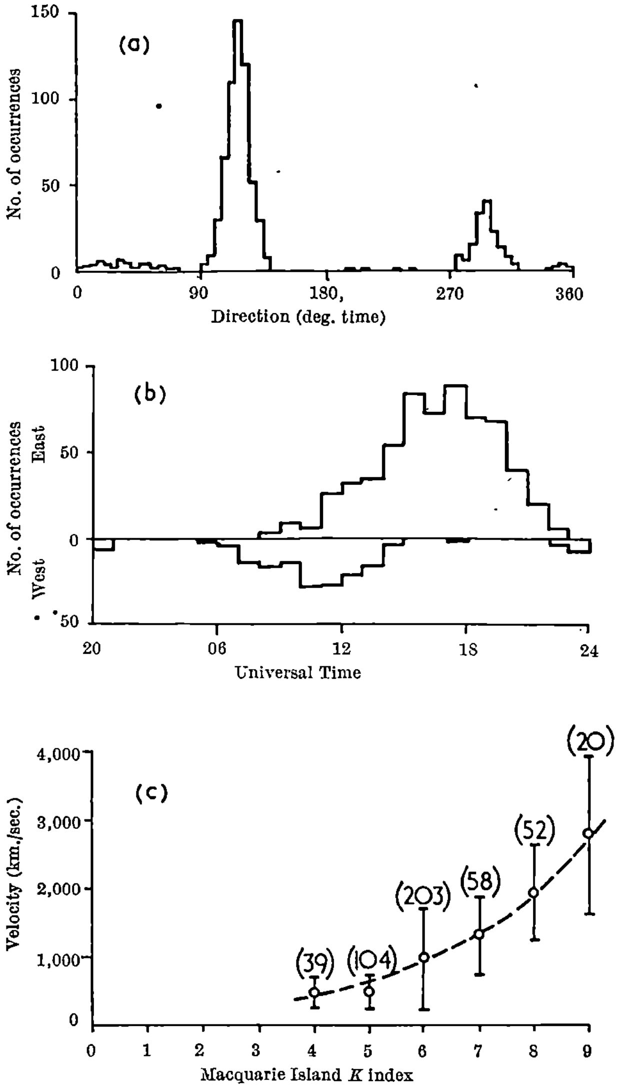

Fig. 2. Movement of echoes: (*a*) Number of occurrences vs. direction; (*b*) number of occurrences containing an easterly or westerly component in the direction vs. Universal Time; (*c*) Average velocities in the 800–1,200 km. range-interval vs. Macquarie Island *K* index. Limits are standard deviations in velocities and bracketed figures are the numbers of cases

occur at any time between about 1030 and 1400 U.T., as shown in Fig. 2*b*. The small number of points between 0 hr. and 0700 hr. U.T. is due to the fact that echoes are normally diffuse at this time[2] and do not reveal sufficient structure on a range–time display to derive an absolute velocity and direction by this method.

There is a wide scatter in the absolute velocities calculated, but in general they increase with the degree of magnetic activity. The average velocities of echoes in the range-interval 800–1,200 km. from the radar are shown plotted against Macquarie Island *K* index in Fig. 2*c*. Macquarie Island is 1,095 km. from radar on an azimuth of 214° geographic.

It has been shown[2] that the echoes come from a layer between a few kilometres and 25 km. thick centred at a height between 110 km. and a little more than 120 km. Recent rocket measurements by Meredith *et al.*[9] at Fort Churchill have revealed the existence of a current at a height of 120 km. during a magnetic disturbance. This evidence, combined with that from previous work discussed above, leaves little room for doubt that the observed movement of echoes can be identified with the magnetic disturbance current system. Following Chapman and Little's view[10] that the average electron density in the auroral zone is 3×10^5/cm.^{3}, a velocity of 1 km./sec. corresponds to a current of 720 amp./km. range for a layer 15 km. thick, assuming the ions are at rest. From Fig. 2*c* a velocity of 1 km./sec. is associated on the average with a K-index of 6 at Macquarie Island. Gadsden[5] has shown that for $K = 6$ the echoes extend to approximately 680 km. from the radar. If we assume further that the near boundary of the echo region corresponds to the boundary of the most intense portion of the disturbance current system, the magnitude of the disturbance vector at Macquarie Island may be found. An approximate calculation gives 375γ for the magnitude in this case, neglecting induced Earth currents. The departure from the quiet day curve for $K = 6$ at Macquarie Island is 360–600γ.

From this preliminary analysis it appears that the ionization giving rise to very high-frequency radar echoes occurs in the most intense portion of the disturbance current system, and that the observed movements of electrons can account for the magnitude of the disturbance vector. This conclusion gives some support to the work of Maeda[11], who found that, in order to interpret the diurnally varying part of magnetic storms by a dynamo theory, a strong polar wind system similar to that deduced here is required. More detailed observations are required to determine whether ions play a significant part.

The work, of which this is a preliminary report, forms part of the research programme of the Dominion Physical Laboratory of the New Zealand Department of Scientific and Industrial Research.

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Atmospheric Tides and Earth Satellite Observations

G. V. GROVES, in a recent communication[1], offered an explanation of the marked change in slope of the periodic time curves of the satellites 1958 β, 1958 δ 1 and δ 2. His suggestion of a relatively sharp discontinuity in atmospheric density on passing from the dark to the light side of the Earth is, however, at variance with the work of Kelvin, Rayleigh and Margules on the ultimate effect of solar heating. From their investigations, one would expect, as

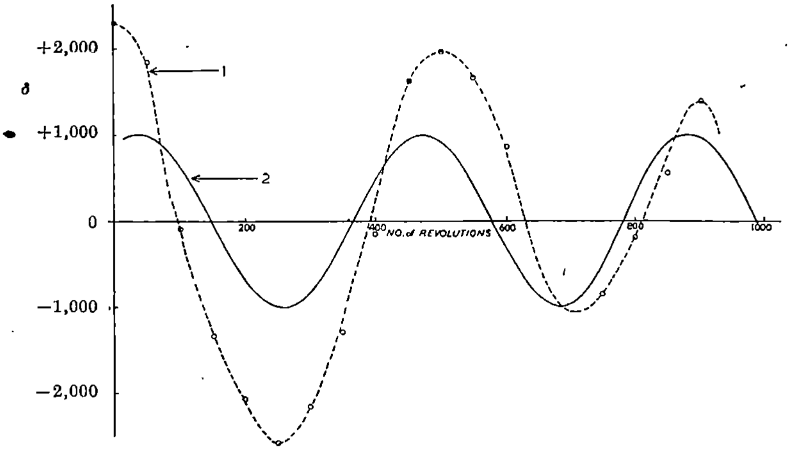

Fig. 1. Satellite 1958 δ 1 ; t_0 = 501·02 days after 1957·0

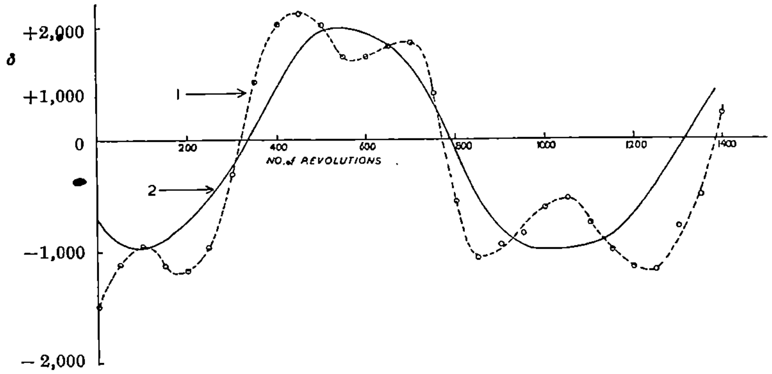

Fig. 2. Satellite 1958 α ; t_0 = 397·16 days after 1957·0

suggested by Kelvin, that the atmospheric distortion produced on the irradiated side of the Earth would lead to a range of Fourier components, that one being most easily detected which corresponded most closely with a natural frequency of tidal waves in the atmosphere. The marked semi-diurnal oscillation in barometric height is ascribed to this effect, and Margules[2] has shown that this corresponds to the natural frequency of waves in a rotating isothermal shell of temperature 298° K.

By a straightforward extension of Margules's analysis, one can investigate the possibility of standing waves of higher multiple frequencies. One finds resonance with the third harmonic in a shell of temperature 470° K., and with the fourth harmonic at a temperature of 590° K. This is relevant to the analysis of observation of satellites, since rocket probes and other sources[3] would suggest temperatures of this order at heights of between one and two hundred miles. More explicitly, one would expect a temperature of 470° K. at a height of about 130 miles, very near the level of the perigee of 1958 δ 1 at the beginning of its life.

In analysing observations of satellites, one has the choice of a variety of parameters, though the periodic time is usually chosen as being the most accurately measurable. Analysis of the dynamics of a satellite orbit under frictional drag, on the other hand, suggests as the most direct parameter the square of the product of the semi-major axis, a, and the eccentricity, e, since it is very nearly a linear function of the time, t. It has the further advantage of being more sensitive to small variations than the periodic time. More precisely, it is convenient to define a parameter u as the ratio ae/a_0e_0 and consider the variation of u^2 as a function of t.

In Figs. 1 and 2, a comparison is given between the departure of u^2 from linearity and the variations to be expected from the third and fourth tidal harmonics respectively. In each case the early part of the orbital development is considered, where u^2 might be expected to be purely linear in form. Only a linear function of t has been subtracted from u^2, the ordinates of the curves 1 being of form $[u^2 - (1 - Kt + C)] \times 10^6$ $(\equiv \delta)$. The comparison curves 2 are the sines of three and four times the difference in right ascension of the Sun and the perigee point respectively.

Fig. 1 refers to the satellite 1958 δ 1 and shows a close agreement between the oscillations of δ and those that might be expected from a third harmonic tide. The sine curve has been given a phase shift of about 70°. One notes further that the oscillations show a decrease in amplitude such as might be expected as the perigee falls out of the region of resonance. The departures of the maxima from precise coincidence are scarcely significant, and are probably the result of a small error in the rate of change of the apex–perigee angle, the effect of which would of course be trebled with the formation of curve 2. The variations of δ nowhere exceed one quarter of a per cent of u, and the regularity of the curve 1 implies a remarkably high degree of precision in the orbital data.

In Fig. 2, for the satellite 1958 α, we find again a close agreement in form between δ and the sine curve, in this case the fourth harmonic with no shift in phase. Superimposed upon the main oscillation in δ is one of much smaller amplitude and higher frequency, which may be identified by its frequency alone as due to an equatorial bulge in the atmosphere of the type caused by the oblateness of the Earth. I have extended my analysis of this effect to meet the criticisms of King-Hele and Leslie[4], and find that this oscillation should have the form :

$$\left(\frac{K}{\omega}\right)\frac{\varepsilon R \sin^2\alpha}{2}\left(\frac{1}{H} - \frac{3}{a_0 e_0}\right)\sin 2\beta$$

where K is the mean value of du^2/dt, ω the mean rate of increase of the apex–perigee angle β, ε and R the ellipticity and radius of the Earth respectively, α the inclination of the orbital plane to the equator and H the scale-height. The amplitude of this oscillation for 1958 α is of order 330 × 10^{-6}, agreeing well with the amplitude of the oscillations demonstrated.

It is difficult to avoid the conclusion that these harmonic tidal waves exist and indeed account for the major anomalies in the orbital observations.

Since the waves are probably operative over a fairly wide vertical range, it is not entirely coincidence that the effects of essentially localized phenomena should appear in two random orbits. As more extended observations become available, it will be of considerable interest to observe the region of decay of the fourth harmonic in the behaviour of 1958 α and the consequent growth of the third harmonic. Such observations would offer a fairly accurate estimate of temperature in the regions of maximum amplitude. Thus we might surmise that the temperature at a height of 224 miles—the perigee level of 1958 α—is of the order of 590° K., implying that the rise in temperature associated with the *F*-layer falls off above 200 miles.

While the major effects modifying the development of satellite orbits are probably now circumscribed, it is a matter of considerable intricacy to predict, for example, the precise values of the periodic time as the orbit develops. On the other hand, the 'young' orbit offers a convenient means for investigating the density distribution of the upper atmosphere.

I am indebted to the Smithsonian Institution for the observations used; without the extreme precision of these values, this discussion would not have been possible.

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From the earliest data on the periods of satellites it was not clear whether the fluctuations in period were due to anything more than the random oscillations of an irregularly shaped body. Changes in the slope of the period–time curves of *Sputniks* 2 and 3 occurred over an interval of a few days, and I remarked that motion of the perigee due to the rotation of the orbital plane seemed to account for the suddenness of the change more easily than the slow drift of the perigee towards the equator. The frequency of these changes seemed related to the crossings of the perigee between the day and night sides of the Earth at three-monthly intervals, suggesting a diurnal variation in air density. As the analysis of data continued, more changes were evident and a periodicity of just less than one month has now been established, and this Parkyn associates with an 8-hr. density variation. The Smithsonian *Sputnik* 3 data, which he presents, show the variation in the period–time curve to be a very smooth oscillation in comparison with earlier data. This is evidence in favour of the phenomenon being a tidal oscillation, and also shows that the effect of the shape of the satellite is mainly averaged out.

One of the first results to be obtained from the launching of satellites was that the air density at 200 km. is several times greater than previously reckoned, due presumably to a higher temperature. Values for the scale-height at 200 km. which I have derived from satellite period–time curves are close to 40 km., and this value is supported by certain rocket measurements. The corresponding temperature is 1,100° K. on assuming the molecular weight for air to be 25 (or 700° K. if we suppose the nitrogen to be almost completely dissociated, which is unlikely). In either case, these values disagree with the values of 470° K. and 590° K., which Parkyn derives from the condition for the third and fourth harmonic oscillations.

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Time Relationship of Metre-Wave and 3-cm. Wave Bursts

It is known that solar bursts are observed over a very large range of wave-lengths. A single burst may extend over a large or small fraction of the range from centimetres to metres. Usually, bursts of strong intensity in the centimetre region are associated with great bursts observed on metre waves. It is generally believed that at the time of these bursts, radial ascension of ionized particles excites radio-frequency radiation at different levels in the solar atmosphere. Moreover, there are reasons for thinking that solar radio waves on the lower frequencies are emitted at a higher altitude in the solar atmosphere than those on the higher frequencies. As a result we observe a regular drift of the onset of the bursts towards the lower frequencies. The object of this communication is to discuss a relation existing between the times of commencement of the bursts observed on 3-cm. waves and on metre waves. This work is based chiefly upon measurements of the associated 3-cm. wave bursts made by means of an interferometer[1].

For this study, the data on metre-wave bursts (200 Mc./s.) provided by the observatory of Nera in Holland have been used. For those 3-cm. wave bursts which are accompanied by precursors, the time of beginning of the precursor has been taken as the time of beginning of the burst.

Fig. 1*a* shows the distribution of the times of commencement of the bursts observed on metre waves relative to those of the associated 3-cm. wave bursts. It will be seen that the metre-wave bursts often follow the associated 3-cm. wave bursts. Our results thus confirm that in the majority of cases the solar bursts are excited by the radial ascension of ionized particles in the solar atmosphere. It is also seen that the delay in time varies between zero and about 20 min. The average delay is about 3 min., corresponding to a velocity of radial movement of the order of 500 km./s.

In order to examine whether the delay in time depends on the dimensions of the bursts, the 3-cm. wave bursts associated with metre-wave bursts have been arbitrarily divided into two classes: (*a*) bursts having at the maximum intensity an apparent diameter less than 1·5 min. of arc on 3-cm. waves, and (*b*) the bursts having at the maximum intensity an apparent diameter greater than 1·5 min. of arc. Figs. 1*b* and 1*c* show the corresponding distributions of the delays of the metre-wave bursts relative to the 3-cm. wave bursts. It is seen that the delay has a tendency to be less for the bursts of smaller apparent diameter. The majority of cases in which the time-difference is small belong to class (*a*), whereas most of the cases observed where the time-difference is great belong to class (*b*). The average value of the delay for these two classes of bursts are of the order of 1 min. and 8 min. respectively. The corresponding velocities of the radial movement are of the order of 1,500 km./s. and 200 km./s. respectively.

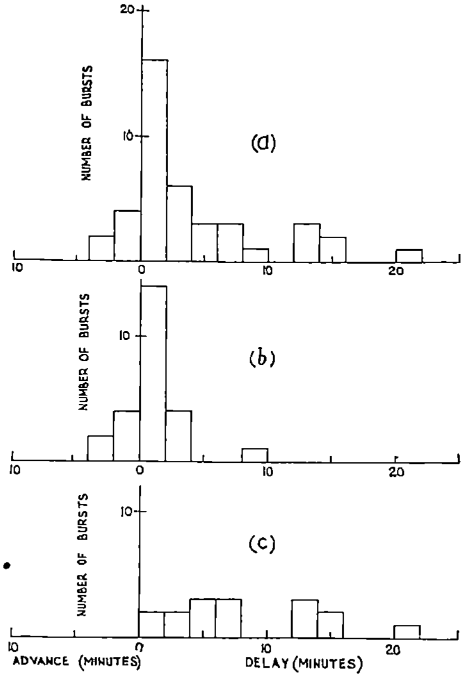

Fig. 1. Distribution of difference in time of commencement of metre-wave bursts relative to associated 3-cm. wave bursts: (*a*) all bursts, (*b*) bursts of diameter < 1·5 min. of arc on 3-cm., and (*c*) bursts of diameter >1·5 min. of arc on 3-cm. radiation

Typical bursts observed on 3-cm. wave-length, the equivalent temperatures of which can reach[2] 10^7 °K., are generally compared with bursts of types II and III usually observed on metre waves. However, it is difficult to identify without ambiguity these 3-cm. wave bursts with one or other of these types. In reality, the comparison between the 3-cm. wave bursts and those observed on longer wave-lengths shows that certain bursts occur almost simultaneously on all the frequencies and are consequently identifiable with bursts of type III. But on metre waves, the bursts of type III last only a few seconds, whereas the bursts observed on 3-cm. waves generally last several minutes. The longer duration of 3-cm. wave bursts agrees better with bursts of type II, which correspond to much greater time delays.

The statistical coincidence of bursts observed on 3-cm. waves and on metre waves shows that the two events have a tendency to occur almost simultaneously, that is to say, correspond to a rapid ejection (at a velocity greater than 1,000 km./s.) when the emissive region is of small diameter, whereas the delay in commencement of metre-wave bursts relative to 3-cm. wave bursts is greater (corresponding to velocities of the order of 500 km./s.) when the emissive region is of large diameter.

The work reported here was carried out at the Meudon Observatory under the guidance of Dr. J. F. Denisse, to whom I express my grateful thanks.

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Feb. 19.

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Atmospheric Dust and Fluorescence

Many chemicals and minerals show a bluish fluorescence that can be destroyed by strong heating but is regenerated, after exposure to the air, by lesser heating[1]; I have called this reversibility of fluorescence by annealing. Stimulated by the well-known experiments of Ewles, I ascribed this to the action of adsorbed water, but recent experiments have shown that this interpretation is not sufficient and that the effect is due to dust most likely of organic origin deposited from the atmosphere; subsequent heating causes an interaction between this dust and the inorganic powder (SiO_2,Al_2O_3) used in these experiments, and this gives rise to stronger fluorescence.

The bluish fluorescence of 'pure' water[2] and of snow[3] is now also found to be due to such dust. For the fluorescence that can be destroyed by heating of magmatic minerals such as many feldspars that show no radiophotoluminescence, adsorbed water (Ewles effect) still seems the most plausible explanation; the presence in these minerals of traces of organic substances is, however, not impossible either, according to Oparin[4].

A more detailed report of this work will appear in the *Wiener Anzeiger*.

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Vienna. Feb. 23.

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The Three-dimensional or Solid-Image Microscope

In a recent communication[1] Gregory and Donaldson describe a prototype microscope which produces a three-dimensional image. In this instrument the microscope and the viewing screen oscillate relative to the object so that the microscope scans the object in depth and the viewing screen follows in phase the real image produced. The frequency of the motion is such that an apparent image of each successive plane is maintained in space without appreciable flicker because of the retention of the image by the eye. Reasonable success was claimed at low magnifications, × 20 being about the greatest useful magnification.

I have experimented with a somewhat simpler apparatus lacking the elegant device of the vibrating image screen. In this case the aim was to increase the depth of field at high magnifications by superimposing on the one virtual image plane, repetitive images of successive planes scanned in depth. This would, for example, allow the contents of a cell to be examined at the one focus under a magnification of × 1,000. Another important use for such an instrument would be the scanning of thick emulsions for particle tracks.

As with Gregory and Donaldson's instrument, the object is held to a sinusoidal oscillation along the optical axis by an alternating magnetic field. The period of the motion is 50 cycles/sec. using a tensioned diaphragm. This is powered by a hollow polarized solenoid surrounding the top of the condenser. The amplitude is controlled with a variable resistance in the low-voltage supply to the vibrator. With the present apparatus a depth of 20µ can be scanned without undue image distortion. However, this is approaching the limit using oil immersion with a 50-cycle/sec. frequency. As Gregory and Donaldson mention, without correction the image in the central region of the scan would be weak, while that at the limits would be very bright by comparison. In the present apparatus the image brightness is rendered uniform by changing the phase so that the lamp brightness is proportional to the velocity of the scanning plane. By suitable adjustment of the impedance of the vibrator supply circuit, this supply is displaced some 80° out of phase with the supply to the microscope lamp. Thus, allowing for the lag in the filament temperature, the brightness increases with the velocity of the scan and falls to a minimum at the end of the stroke where the velocity is momentarily zero. Further critical control can then be exercised by varying the current to the lamp, thus altering the hysteresis in the filament.

The apparatus can be adjusted to give surprisingly good resolution at magnifications of × 1,000, using oil immersion objectives, provided that amplitudes less than about 15μ are used. No trouble was experienced with non-drying immersion oils of normal viscosity. The main difficulty at present is that standing waves and other imperfections leading to non-linear motion are present in the vibrator diaphragm. These may be corrected for any position; but readjustment is required with each new position of the slide. The inherent problem is to provide strictly linear motion without increasing bulk or momentum.

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GEOPHYSICS and GEOCHEMISTRY

Remanent Magnetism of the Cretaceous Basalts of Madagascar

A general study of the remanent magnetism of volcanic rocks from Madagascar has been undertaken since the beginning of 1958 under the direction of Dr. H. Besairie, chief of the Geological Department of Madagascar.

From various places in the island, more than a hundred oriented samples have been collected by one of us (L. C.) and seven samples by J. Boulanger and P. Bussiere. Forty samples belong to flows or dykes well dated from the upper Cretaceous. Their ages have been proved to vary between Cenomanian and Santonian[1].

The samples were taken in places widely distributed along the eastern coastal district and the western part of the island. They were generally collected in quarries or trenches, some metres below ground-level, but sometimes at ground-level in river beds. The rocks are dolerites, basalts or sakalavites.

In some places, Ampijoroa, Amborompotsy, Antsalova (part), the directions, as well as the values of the intensities of magnetization, proved widely scattered. Values as high as 33 × 10^{-3} c.g.s. units/gm. were found. It is believed[2,3] that lightning currents were responsible for these magnetizations. For the other places the intensities as well as the directions of magnetizations showed good consistency.

For samples originated from the same flow or dyke, the differences between the individual values obtained and the mean value vary from 0 to 4 deg. for inclination and from 0 to 20 deg. for declination.

According to the places, the mean values found for the intensities of magnetization vary from 0·8 × 10^{-3} to 9 × 10^{-3} c.g.s. units/gm.

The magnetic stability of the samples was tested by E. Thellier's method[4], that is, turning over the sample in the Earth's magnetic field for one to several months and comparing the values obtained before and after turning over. Except for two samples, the magnetization showed no variation.

The nature of the magnetization was tested on some samples by successive heatings in a non-magnetic furnace. Only one Curie point was observed between 400° C. and 600° C. for each sample. The magnetization is thought to be thermoremanent[5] and acquired at the time of cooling of the rocks.

All the samples are magnetized according to the sense of the present geomagnetic field at Madagascar. The mean values of the directions of magnetization for the stable samples at each place are given in Table 1. The inclinations are termed negative when the extremity of the magnetization vector points above the horizon.

Table 1

	Inc.	Dec.
Northern districts		
Sambava	−49° 30′	15° E.
Antalaha	−55°	39° E.
Samanavaka	−48°	18° W.
Central districts		
Fenerive	−62°	19° E.
Andramy	−51°	7° E.
Andafiha	−57°	18° E.
Antsalova	−47°	4° E.
Southern districts		
Manakara	−70°	30° E.
Vineta	−53°	26° E.
Tongobory	−56°	15° E.

The inclinations are systematically steeper by 2–10 deg. than those of the present magnetic field for the places on the eastern coast (Sambava, Antalaha, Fenerive, Manakara), but generally lower for the western districts (the differences from the present magnetic field being less than 7 deg.). Notwithstanding a dispersion of some degrees, the magnetic inclination of the samples increases with increasing latitude.

On the whole there is not much difference between the distribution of the magnetic inclination of the samples and that of the present geomagnetic field in the island, as we noticed in our first studies.

The declinations of the samples are all easterly, except for one place (Samanavaka). They differ widely from those of the present geomagnetic field in the island (which vary from 7° W. to 19° W.), the mean difference being nearly 30 deg.

The calculation of the orientation of the dipole axis corresponding to the magnetization of the rocks gave the values for the co-ordinates of the north geomagnetic pole as shown in Table 2.

Table 2

	Lat.	Long.
Northern districts	70° N.	161° W.
Central districts	70° N.	165° W.
Southern districts	64° N.	177° W.
Mean	68° N.	168° W.

The place calculated is in the vicinity of the Behring Strait (Fig. 1). S. K. Runcorn[7] has given results he obtained from the Cretaceous Dakota Sandstones the magnetization of which could correspond to a north geomagnetic pole at latitude 77° N. longitude 127° E., the sense of magnetization being

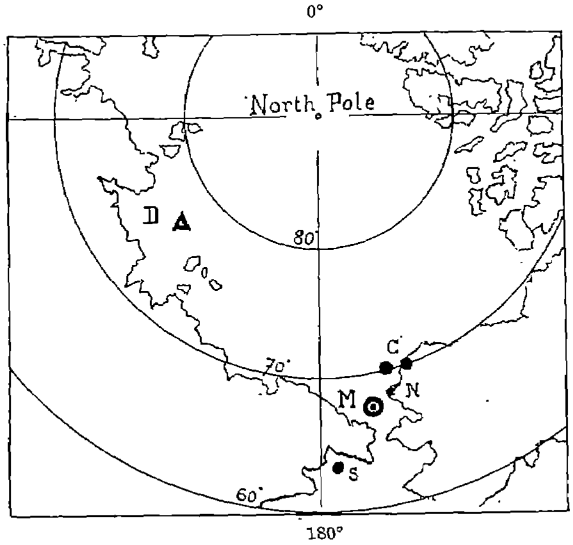

Fig. 1. North geomagnetic poles for Dakota (*D*, △); Madagascar, mean (*M*, ⊙); Madagascar, parts (*N*, *C*, *S*, ●)

reversed compared with that of the present terrestrial magnetic field.

The north geomagnetic pole for Madagascar is thus at a distance of less than 1,500 miles from the north geomagnetic American pole as given by Runcorn, and a little farther from the present geographical north pole.

This can be interpreted in different ways.

(1) The geomagnetic field, though having a dipole character for the main part, may have presented at times in the past a more or less complicated pattern, and the anomalies were smoothed out by taking the means of values scattered over long periods (of perhaps thousands or millions of years).

Therefore our results would have no significance in the perspective of polar wandering or continental drift.

(2) According to Runcorn's hypothesis[8], the mean geomagnetic field obtained by taking the mean of values scattered over a long period is a geocentric dipole field; our results would give the mean orientation of the dipole relative to Madagascar during a part of the upper Cretaceous.

(*a*) If the axis of the dipole had undergone, in the past, angular displacements of limited amplitude comparatively rapidly, say, for example, 10–20 deg. in one or a few million years, then the difference between our results and those of Runcorn could be most simply interpreted by the fact that the samples of America and of Madagascar do not belong exactly to the same period and the results give a picture of the orientation of the dipole at two different periods of the Cretaceous.

The opposed polarities of magnetization for the samples of Dakota and Madagascar give support to this hypothesis.

(*b*) If the dipole axis has undergone in the past displacements only at a slow rate (whether the dipole coincided or not with the axis of rotation of the Earth), we would have to think of relative continental drift for Madagascar and North America. From the Cretaceous up to the present time, according to calculation, the drift for Madagascar would have been about 1,500 miles in amplitude with a direction north-north-easterly.

Though displacements of much larger amplitude have been contemplated for Australia[9] and the Deccan peninsula[10], this hypothesis is considered by us as less likely than that of paragraph 2*a* above.

We wish to express our thanks to Prof. E. Thellier, whose advice was of inestimable value, and to Dr. H. Besairie, who has organized the sampling part of the work and provided the stratigraphical dating. We are also indebted to Prof. H. Dessens, director of the Puy de Dôme Observatory, and to Prof. M. Roques, who have greatly facilitated these studies.

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Biological Origin of Manganese-rich Deposits of the Sea Floor

Recently, one of us has advanced arguments[1] in support of the idea that manganese-rich deposits of the sea floor may result from the metabolic activity of a bottom-dwelling organism that derives its nutrients from organic complexes in the water. We present here some new evidence that is relevant to that concept.

On December 18, 1958, at lat. 34° 48′ N., long. 60° 30′ W., in 5,139 m. of water, Mr. L. V. Worthington on *Chain* Cruise No. 2 retrieved about 50 gm. of light tan mud and preserved it for us in borate-buffered (*p*H 8) formalin. The present bottom temperature at this site is 2·3° C. The finer fractions of this material were removed by suspension in water and decantation, and it was possible to isolate a few mgm. of a relatively coarse fraction, which, for the most part, consists of the vacant tests of agglutinated arenaceous (? *Rhabdammina* sp.) and of calcareous Foraminifera. It is of particular interest that almost all the former are coated inside and out with a dark brown or black, earthy or shiny veneer which, by one-dimensional paper chromatography, is seen to be markedly similar in composition to manganese-rich nodules from the Blake plateau, that is, containing appreciable quantities of nickel, cobalt and copper as well as abundant manganese and iron. Treatment with 6 *N* hydrochloric acid removes the dark coating and leaves the Foraminifera tests intact, thus demonstrating that the manganese-rich material was formed as a surface deposit, and not through the capture of pre-existing manganese-rich particles by the living Foraminifera. All manganese-rich particles in this sample apparently were formed by deposition on agglutinated Foraminifera the natural surfaces of which seem to be studded with detrital quartz grains; no comparable manganese-rich deposits are visible on calcareous tests or on isolated sand grains. That the uncoated agglutinated Foraminifera have on their surfaces some protein-rich material is suggested by their adsorption of rose bengal dye[2], and by their reaction with ninhydrin.

To us, these observations support the argument that manganese-rich deposits of the sea floor originate through biological rather than inorganic processes. It would seem that the protein-rich exudate of these agglutinated Foraminifera has provided a favourable substrate which promoted the growth of a colony of organisms that are capable of extracting trace elements from sea water. Siliceous detrital grains on the sea floor, that were lacking in the protein-rich coating, were not such biologically attractive sites, nor were the calcareous tests of other associated Foraminifera.

We are now making preparations for a careful search for the organism which, we expect, is responsible for this type of deposition of trace elements from sea water.

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BIOCHEMISTRY

Amino-Acetone : its Isolation and Role in Metabolism

A PRELIMINARY study[1] of the properties of a metabolite produced by washed suspensions of *Staphylococcus aureus* led to the provisional assignment of the structure $CH_3.CO.CH_2NH_2$. This compound, hitherto undetected in Nature, has now been isolated in crystalline form and positively identified as amino-acetone.

The present communication is concerned with the broad details of the isolation and characterization of amino-acetone and, in addition, presents a hypothesis which accounts for its formation and catabolism. It is suggested that this latter involves glyoxalase, an enzyme system which, as yet, has been without a definitive role in intermediary metabolism.

The accumulation of amino-acetone by *Staph. aureus* cells harvested from a bulk culture medium and suspended in phosphate buffer (pH 7·0) containing 0·02 *M* DL-threonine was measured at intervals using a modified picrate reaction method[2,3]. During a 20-hr. incubation a total of 15 m.moles of the compound was produced ; it was isolated by adsorption and elution from 'Amberlite *IRC* 50', fractionation with phosphotungstic acid and finally by chromatography on paper. It was obtained as the pure compound by precipitation from ethanol, as the salt of p-toluene sulphonic acid. This salt was recrystallized twice from absolute ethanol–diethylether as fine white needles—yield 0·39 gm. (m.p. 130·5°).

Elementary analysis gave the following results : amino-acetone p-toluene sulphonic acid salt ; C, 49·2 ; H, 6·3 ; N, 5·9 ; S, 13·0. $C_{10}H_{15}O_4NS$ requires : C, 49·0 ; H, 6·2 ; N, 5·7 ; S, 13·1 per cent.

Amino-acetone hydrochloride was synthesized via acetonylphthalimide[4] and converted to the p-toluene–sulphonic acid salt. This was recrystallized twice from absolute ethanol–diethylether and yielded long thin leaflets with m.p. 130·5°. On analysis it gave the following data : C, 49·2. H, 6·4 ; N, 5·9 ; S, 12·9 per cent. A mixture of the synthetic material, and that isolated from the culture, also melted at 130·5°.

The behaviour of the natural and synthetic materials was identical when chromatographed on paper in a number of solvent systems and when subjected to paper electrophoresis. The identical nature of both products was also confirmed by infrared spectroscopy, which was kindly carried out by Dr. E. Spinner.

It was shown[1] that a compound, now identified as amino-acetone, was formed by *Staph. aureus* either rapidly from threonine alone or slowly from glycine plus glucose, oxygen being necessary in both cases. The question now arises as to the mode of formation of amino-acetone from the two amino-acid precursors. In the case of glycine it would seem likely that it condenses with an acetyl derivative to give α-amino-β-ketobutyric acid in a manner analogous to the formation of α-amino-β-ketoadipic acid from a succinyl derivative and glycine, by the pathway proposed for the synthesis of δ-aminolævulinic acid[1,5–7]. Thus it is envisaged that acetyl-coenzyme *A*, derived from glucose, condenses with glycine as shown in equation 1. The α-amino-β-keto acid so formed would then give rise to amino-acetone by a simple decarboxylation (equation 3). In this connexion it is of interest to note that Gibson *et al.*[5] have independently reported the formation of an amino-ketone from acetyl-coenzyme *A* and glycine by red blood cell preparations. In the case of threonine, a dehydrogenation reaction would yield α-amino-β-ketobutyric acid (equation 2) from which amino-acetone would arise as before.

$$CH_3.CO.S\text{—}CoA + CH_2NH_2.COOH \rightarrow CH_3.CO.CHNH_2.COOH + CoA\text{—}SH \tag{1}$$

$$CH_3.CHOH.CHNH_2.COOH \xrightarrow{-2H} CH_3.CO.CHNH_2.COOH \tag{2}$$

$$CH_3.CO.CHNH_2.COOH \rightarrow CH_3.CO.CH_2NH_2 + CO_2 \tag{3}$$

Regardless, however, of the actual mechanisms involved in the formation of amino-acetone, the appearance of this compound does suggest a role in metabolism, especially as it is known that amino-acetone labelled with carbon-14 is oxidized to $^{14}CO_2$ in the rat[8]. It is suggested that the above facts may be integrated into a metabolic cycle (Fig. 1) which could have a widespread occurrence in animal and bacterial cells.

It is postulated that amino-acetone, formed by the routes described above, is deaminated either by oxidation or transamination to yield methylglyoxal. If formed, methylglyoxal would be rapidly converted to D-lactic acid by glyoxalase and thence to pyruvic acid by the D-lactate dehydrogenase system[9–11]. Both these enzyme systems have a wide distribution in bacteria and in animal tissues.

The postulated cycle provides a new route for the oxidation of threonine and glycine and, in the latter case, an alternative to the succinate–glycine cycle[7]. In addition, it provides an interesting feature, namely, a possible source of substrate, and indeed a purpose, for glyoxalase, an enzyme system the place of which in the metabolic picture has been a puzzle for many years.

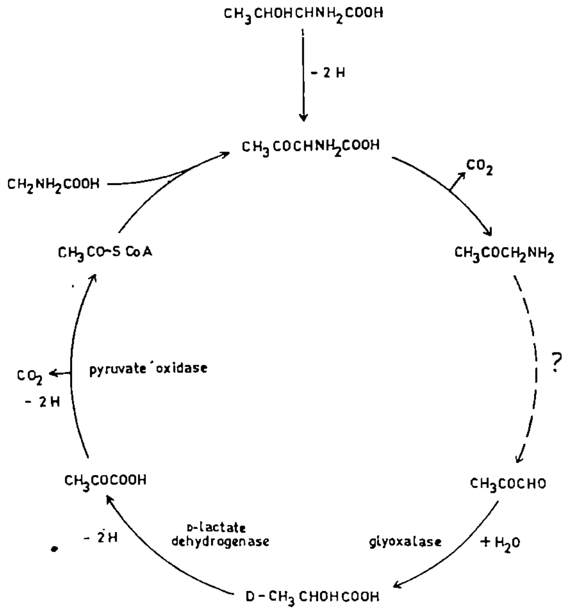

Fig. 1. Postulated amino-acetone cycle. The interrupted line represents a possible deamination reaction

The accumulation of amino-acetone in cultures of *Staph. aureus* is presumably due to the inability of this organism to deaminate the compound. Such a metabolic defect would be entirely in keeping with the limited nitrogen metabolism implied by the strict amino-acid requirements of *Staph. aureus*.

Experiments to test the validity of the above hypothesis are now in progress and, as with full details of the present work, will be reported later.

I wish to thank Prof. A. H. Ennor for the constant encouragement and advice which he has given throughout the course of this work.

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Identification of Barbiturates

In Great Britain the most common poisons at the present time are the 5 : 5′ disubstituted barbiturates. The longer-acting barbiturates, barbitone and phenobarbitone, can accumulate in the body when administered in relatively low therapeutic dosage, and concentrations of these drugs in the blood of about 5 mgm./100 ml. do not necessarily imply poisoning. The shorter-acting barbiturates, when taken in therapeutic quantities, however, do not accumulate, and in such cases this concentration would imply that an excessive quantity had been taken.

The only reliable method for the quantitative assay of barbiturate in 5–10 ml. samples of blood is ultra-violet spectrophotometry. The optical density difference at 240 mμ of aliquots at *p*H 10 and *p*H 2 is measured, and, because the E(1 per cent, 1 cm.) values for the various barbiturates are very similar, the total barbiturate concentration can be obtained. In order to assess the likely effect of this concentration it is necessary to identify the ingested barbiturate or at least assign it to the long- or short-acting group. Although slight differences in spectra between the various barbiturates can be detected and used for identification purposes[1], they are of value only if the background absorption is minimal and one barbiturate is present.

It is the purpose of this communication to direct attention to a test which has proved valuable in assisting in the identification of the various barbiturates. Maynert and Washburn[2] showed that concentrated sulphuric acid at room temperature dealkylated some secondary alkyl groups in the 5 : 5 disubstituted barbiturates, and Brooker[3], using treatment with acid at 100° for 1 hr., separated by paper chromatography the products from pentobarbitone and amylobarbitone. Combination of the techniques used by these workers has shown that if the products of the acid treatment at 100° for 1 hr. are, after dilution with water and extraction into ether, examined by ultra-violet spectrophotometry using 0·5 N aqueous ammonia as the solvent, then rapid and easy differentiation of several barbiturates is possible. The results of such treatment on the barbiturates commonly prescribed in the United Kingdom are shown in Table 1.

Table 1

	Result of treatment	λ Maximum of product in 0·5 N ammonium hydroxide
Barbitone Amylobarbitone (amytal) Butobarbitone (soneryl)	Unchanged	240 mμ
Pentobarbitone (Nembutal) Cyclobarbitone (phanodorm)	Attacked	268 mμ
Quinalbarbitone (seconal)	Attacked	Very weak absorption at 240, 266 and 315 mμ
Phenobarbitone	Completely destroyed	Nil

The products from the dealkylation of 'Tuinal' (mixed amylobarbitone and quinalbarbitone) give detectable absorption maxima at 240 mμ and 315 mμ. The absorption from the treatment of seconal is, however, very low and the 315 mμ peak is usually only observable when the extracts are reasonably pure.

The tungstic acid precipitation method followed by isolation of the weakly acidic ether-soluble fraction gives excellent products.

These techniques, coupled with those of paper chromatography[4], have, as yet, not failed to identify unambiguously any of the barbiturates involved in more than one hundred cases submitted to this laboratory in which therapeutic or toxic doses had been ingested.

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Isomerization of Poly-*cis*-carotenes by Chlorophyll *in vivo* and *in vitro*

One of the *Chlorella* mutants described by Claes (strain 5/520)[1] synthesizes in the dark certain poly-*cis*-isomers, which are described in the literature as protetrahydrolycopene[2] and prolycopene[3]. In the algal cells the stereoconfiguration is sensitive to light. If oxygen is present, the procarotenes are isomerized in blue but not in red light, yielding the *trans*-forms in the cells. In this case light absorbed by the carotenes is presumed to be responsible for their isomerization.

Not so readily explained was the observation that in the mutant 5/520 the stereoconfiguration of protetrahydrolycopene and prolycopene can become unstable also in red light, which is not absorbed by carotenes. This phenomenon requires irradiation in a nitrogen atmosphere, absence of oxygen alone being insufficient[4].

In view of more recent results, the isomerization of protetrahydrolycopene and prolycopene under conditions of anaerobiosis and red light appears to be sensitized by the chlorophyll present in small amounts in the dark-grown mutant. After chromatographic isolation, both procarotenes show the same behaviour in petroleum ether as in the cell, if the solutions contain some chlorophyll.

Fig. 1 shows the chlorophyll-sensitized isomerization of protetrahydrolycopene in red light (500-W. tungsten lamp, Schott filter *RG* 1 and *KG* 1, distance of the solution from the light source about 60 cm.). Irradiation for 2 hr. results in a change from the spectrum of protetrahydrolycopene to one predominantly that of *trans*-tetrahydrolycopene. If the solution contains no chlorophyll, the procarotene spectrum is scarcely changed under the same conditions of irradiation.

As in the intact cells, chlorophyll-sensitized isomerization of poly-*cis*-carotenes in petroleum ether is inhibited by oxygen. Fig. 2 shows the influence of aeration on the isomerization of prolycopene. The carotene solution contained chlorophyll *a* and was irradiated with red light in the presence of nitrogen or air. Whereas the isomerization is almost at equilibrium after irradiation for half an hour in nitrogen, the presence of oxygen is inhibitory.

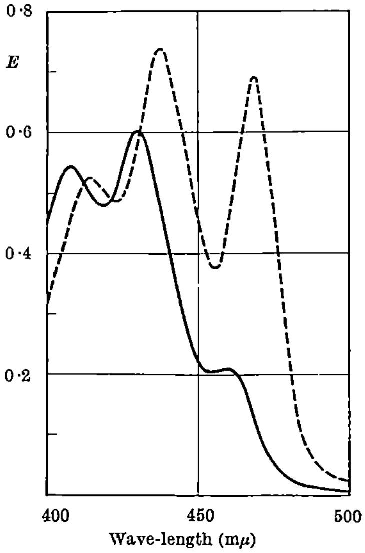

Fig. 1. Absorption spectrum of a mixture of protetrahydrolycopene ($6 \cdot 1 \times 10^{-6} M$) and chlorophyll *a* ($0 \cdot 9 \times 10^{-6} M$) in petroleum ether before, ——, and after, - - - -, irradiation for 2 hr. with red light

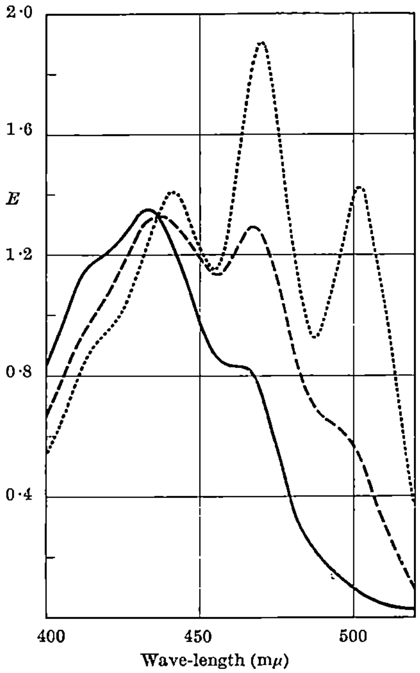

Fig. 2. Absorption spectrum of a mixture of prolycopene ($1 \cdot 2 \times 10^{-5} M$) and chlorophyll *a* ($0 \cdot 2 \times 10^{-5} M$) in petroleum ether before, ——, and after irradiation for half an hour with red light in the presence of nitrogen, ... , or air, - - - -

These findings indicate that in certain conditions (oxygen deficiency and light) the stereoconfiguration of carotenoids in the chloroplasts might be controlled by chlorophyll. The reaction is not limited to the structure of chloroplasts and can be observed outside the cell in pure solutions. Further implications necessarily await more detailed studies of chlorophyll – carotenoid interactions in general.

We are indebted to Miss I. Dobrigkeit for technical assistance.

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Green Fluorescence of Guanidinium Compounds with Ninhydrin

Currently available methods for the determination of creatine and other guanidinium compounds are based on non-specific chromogenic reactions. These include the Jaffe, the diacetyl α-naphthol, the Sakaguchi, and the sodium nitroprusside–potassium ferrocyanide reactions. Determination of the individual members of the guanidinium group requires chromatographic separation, chemical degradation, or specific enzymatic destruction of the compound. In a search for a more satisfactory reaction for detection of guanidinium compounds than is at present afforded by chromogenic reactions we have found that ninhydrin (1,2,3-indantrione hydrate) in strongly alkaline media forms highly fluorescent products with guanidine and monosubstituted or N,N-disubstituted guanidines. The most highly fluorescent product is formed with creatine, which can be determined in concentrations as low as 0·07 μgm./ml.; other guanidinium compounds form less fluorescent products.

The Farrand spectrofluorometer model *A*, calibrated by the method of Sprince and Rowley[1], was used for determining excitation and fluorescence spectra. In all determinations, 2 ml. of 0·5 per cent ninhydrin in water and 2 ml. of 1·0 *N* potassium hydroxide were added successively to 2 ml. of an aqueous solution of the guanidinium compound. All measurements were made at 24° C., and the sample was shielded from light except when fluorescence was measured.

Immediately upon the addition of potassium hydroxide to a solution of ninhydrin the five-membered ring is opened to form *o*-carboxyphenylglyoxal[2]. It is apparently the latter compound which combines with the guanidine group to give the fluorescent product; however, any excess *o*-carboxyphenylglyoxal interferes with fluorescence measurements by strongly absorbing the excitation wavelengths used. In the strongly alkaline solution excess *o*-carboxyphenylglyoxal is degraded to *o*-carboxymandelic acid[2], which is colourless, non-fluorescent, and has negligible absorbance at the excitation and fluorescence wave-lengths. Thus it is necessary to delay fluorimeter readings until this excess has been degraded and fluorescence reaches a maximum. With 0·5 per cent ninhydrin and 1·0 *N* potassium hydroxide a plateau of constant fluorescence occurs 9–14 min. after addition of alkali, during which time satisfactory fluorimeter readings may be made. Fluorescence decays to about half the initial value after 1 hr. and to 1/40 after 24 hr. Exposure to sunlight or to higher temperatures accelerates the rate of destruction of the fluorescent material.

The addition product of a guanidinium compound and ninhydrin is a highly fluorescent material with two sharp excitation peaks, at 305 and 390 mμ, the fluorescence at 390 mμ being approximately twice as intense as that at 305 mμ (Fig. 1). The fluorescence spectra have maxima at 495 mμ (Fig. 2). The spectra are similar for the guanidinium compounds tested; however, the amplitude of the peaks varies with the compound. It appears that N,N-disubstituted guanidines form the most highly fluorescent compounds, unsubstituted guanidine the least fluorescent, while monosubstituted guanidines are intermediate. The fluorescence of creatine, using an excitation wave-length of 390 mμ and measuring fluorescence at 495 mμ, is linear from 0·5 μmole to 75 μmole per litre.

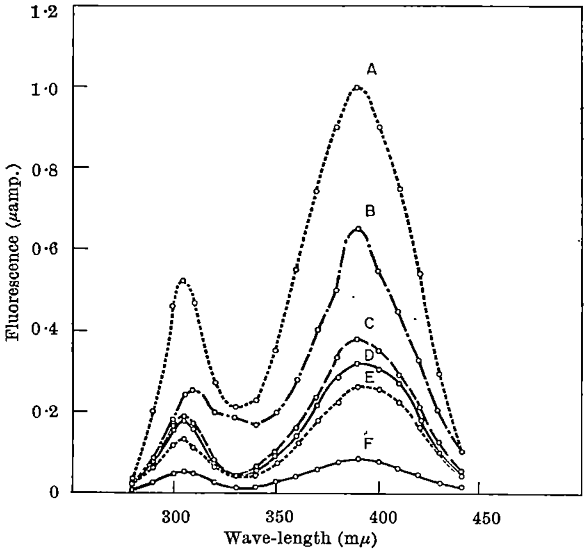

Fig. 1. Excitation spectra of the guanidinium compounds: *A*, creatine; *B*, dimethylguanidine; *C*, guanidoacetic acid; *D*, methylguanidine; *E*, arginine; *F*, guanidine. Each solution contains equal volumes of 0·5 per cent ninhydrin, 1·0 *N* potassium hydroxide and a 50-μmoles/l. solution of the guanidinium compound

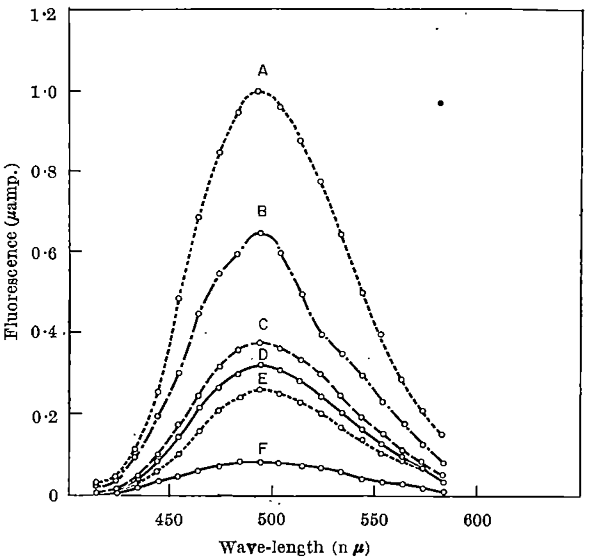

Fig. 2. Fluorescence spectra of the guanidinium compounds. Solutions are the same as for Fig. 1

Apart from the compounds the fluorescence spectra of which are presented in Figs. 1 and 2, creatine phosphate, creatinine, guanine and urea were studied. The fluorescence of creatine phosphate is less than 1 per cent, and the fluorescence of creatinine less than 0·5 per cent of that of an equimolar concentration of creatine. A saturated aqueous solution of guanine gives no fluorescence, nor do ammonium salts in concentrations 100 times that of the guanidinium compounds studied. Urea gives about 1/50,000 the calculated fluorescence of an equimolar concentration of creatine.

In his studies of ninhydrin, Ruhemann[2] noted that guanidine combines with the hydrated 2-carbonyl group of ninhydrin to give a red addition product in alkaline solution. This probably is not the structure of the fluorescent compound, since it appears that formation of the fluorescent addition product occurs after the five-membered ring of ninhydrin is opened, as indicated by the loss of the usual colour reactions of ninhydrin. It appears that the reaction requires at least one free NH_2 group on the guanidinium compound since guanine, creatine phosphate and creatinine do not form the fluorescent addition product. The combination probably occurs at one or both of the adjacent ketone groups of *o*-carboxyphenyl-glyoxal since the yellow colour of this compound caused by the adjacent ketone groups disappears when the addition product is formed.

Although the fluorescent reaction is non-specific among the guanidinium compounds, it provides a marked increase in sensitivity over the chromogenic reactions currently used for the determination of these compounds. Application of the reaction to the determination of creatine and creatine phosphate in biological material is now being studied.

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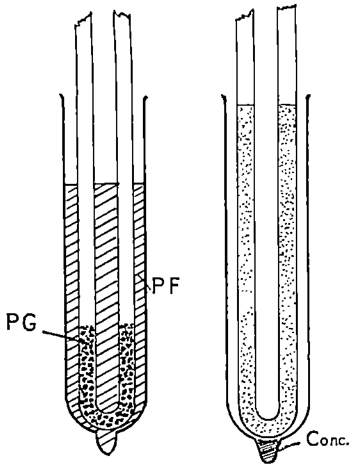
A Simple Method for the Concentration of Fluids containing Protein

THIS method is essentially based on the well-known principle of dialysis against substances of high molecular weight.

Fluid containing protein is placed in a glass tube or container, preferably with a small protuberance at the bottom end having approximately the smallest volume to which the fluid is to be concentrated. The size and shape of the glass container should be such as to provide the greatest possible dialysing surface. Using small glass tubes and narrow tubing, even a few millilitres of fluid containing protein can be successfully concentrated. The polyethylene glycol ('Carbowax' 20 *M*, made by Union Carbide, also available from G. T. Gurr), a waxy, flaky substance, with a molecular weight of 20,000, is broken up and an appropriate quantity of the dry granulated material is poured into the dialysis tubing. This can easily be achieved by inflating the tubing and using a funnel. 'Visking' dialysis tubing was used throughout, but any similar tubing would be suitable. The proportion of polyethylene glycol to fluid containing protein is not critical, but there should not be less than 1 part of polyethylene glycol to 10 parts of fluid. Polyvinylpyrrolidone (PVP) in dry powder form was also tried and gave satisfactory results; it is, however, much more expensive. The dialysis tubing containing the polyethylene glycol is then bent double (or more) and is placed in the glass vessel containing the glycol (Fig. 1). The length of the tubing should be such as to allow for the rising column of water inside it. It is advisable to moisten the polyethylene glycol inside the tubing with a small quantity of water just before it is placed in the fluid containing protein. The level to which the tubing should be pushed down depends on the final concentration required. The concentrating process ceases, of course, when the fluid containing protein reaches the level of the bottom of the tubing. The whole procedure is thus automatic. With larger quantities of fluid the tubing can be bent several times, providing a larger dialysing area and accelerating the process. The electrolyte content of the concentrate will be the same as in the fluid containing protein at the start, as there is a free passage of electrolytes across the membrane.



Before After

Fig. 1. Apparatus for concentrating fluids containing protein. *PF*, fluid containing protein; *PG*, polyethylene glycol; *Conc.*, concentrate

The method is rapid, reliable, and no special equipment is required. It has also the great advantage that the concentrate can be collected from clean glass and need not be scraped out from the inside of a sticky tube. Under suitable conditions a concentration, for example, of 10 ml. of urine to about 0·25 ml. is easily achieved in 3–4 hr. The high efficiency of the method is also due to the fact that the hydrophilic agent, namely, polyethylene glycol, does not contain water and has, therefore, full absorptive capacity. No denaturation effects were observed.

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Unfermentable Sugars in Barley Mash fermented by the Amylo Process

IN an earlier communication[1] concerning the production of alcohol from starchy materials by the amylo process, it was demonstrated that sugar consumption with barley fell considerably below that of the other raw materials by failing to exceed 85 per cent even with barley grains from which the bran had been removed. This was attributed to the presence of a considerable amount of unfermentable sugars. We now wish to report on the composition of residual unfermentable sugars in the fermented mash of barley, including the isolation of laminaribiose and of a β-linked glucosyl trisaccharide from this mash.

Polished barley grains were cooked with 0·03 per cent hydrochloric acid at 3 kgm./sq. cm. for 60 min. Alcohol fermentation of the cooked mash (total sugar 10·9 per cent) was carried out by the amylo process with the amylo mould (*Rhizopus javanicus* Takeda) and alcohol yeast (*Saccharomyces cerevisiae* sp.). After completion of fermentation, the mash (total residual sugar 1·6 per cent) was deproteinized and concentrated *in vacuo*. The acidic hydrolysis of this concentrate produced pentose (xylose and arabinose) and glucose as the sugar components detectable by paper chromatography; the pentose–glucose ratio of 44 : 56 was estimated on the basis of the paper chromatographic analysis devised by A. E. Flood *et al.*[2]. The concentrated sugar mixture (300 ml.) equivalent to 4,000 ml. of fermented mash was then separated into xylose, arabinose, galactose (?), three pentosyl oligosaccharides, five glucosyl oligosaccharides and higher pentosyl and glucosyl oligosaccharides by a combination of carbon column[3] and paper chromatographic techniques. Three pentosyl oligosaccharides had R_F

values of 0·29, 0·17 and 0·06 in *n*-butanol/pyridine/water (6 : 4 : 3), respectively. Further investigation on the structure of these pentosyl oligosaccharides was not carried out. Five glucosyl oligosaccharides consisted of two minor components presumed to be *iso*maltose (or gentiobiose) and kojibiose (or cellobiose), and three major constituents (*a*, *b* and *c*) having R_F values of 0·29, 0·16 and 0·05 in the same solvent, respectively. The ratio of *a*, *b* and *c* in the fermented mash was shown by paper chromatographic analysis to be 18 : 48 : 34. The greater part of each of these three sugars was eluted in the pure state (paper chromatography and ionophoresis[4]) from the carbon column ; yields, 1·1 gm. of sugar *a*, 2·8 gm. of sugar *b* and 2·5 gm. of sugar *c*.

Sugar *a* was crystallized from methanol. The crystals were recrystallized from the same solvent : melting point 205–208°, unchanged on admixture with an authentic specimen of α-laminaribiose, $[\alpha]_D^{16} = +24\cdot8 \rightarrow +18\cdot8°$ (*c*, 2·5 in water). Acetylation of a portion of the free sugar yielded the crystals. The crystalline acetate was recrystallized from 95 per cent ethanol ; melting point, 160·5–161·0°, undepressed on admixture with authentic β-octaacetate, $[\alpha]_D^{16} = -28\cdot8°$ (*c*, 2·5 in chloroform).

Sugar *b* was reducing and showed $[\alpha]_D^{16} = +10°$ (equil. : *c*, 3·0 in water). Acidic hydrolysis of sugar *b* gave only glucose on the paper chromatogram (identified as β-pentaacetate). From R_F and the elution behaviour from the carbon column, this substance was presumed to be a trisaccharide. A further indication was that the degree of polymerization calculated from the increase of reducing power[5] after hydrolysis was 2·8. The substance (1 gm.) was submitted to partial acidic hydrolysis with 1·0 per cent sulphuric acid at 100° for 2½ hr. Carbon column chromatography of the solution produced the mixture of disaccharides together with glucose and parent sugar. This mixture was fractionated by chromatography on paper into two components ; the faster-moving component (0·11 gm.) and slower-moving component (0·1 gm.). Both were characterized by conversion into β-laminaribiose octaacetate and β-cellobiose octaacetate, respectively. This result showed that sugar *b* contained laminaribiose and cellobiose moieties. The sequence of linkages was determined by sodium borohydride reduction of sugar *b* to the sugar alcohol and partial acidic hydrolysis of the product. Paper chromatographic analysis revealed that the only reducing disaccharide present was cellobiose, thus proving that sugar *b* was O-β-D-glucopyranosyl-(1 → 4)-O-β-D-glucopyranosyl-(1 → 3)-D-glucose. It also supported the above structure that laminaribiose was the only disaccharide produced by the partial hydrolysis of β-glucosidase (almond emulsin)[6].

Acetylation was carried out with sodium acetate and acetic anhydride at 125–130° for 40 min. Crystalline β-hendecaacetate was formed from 95 per cent ethanol : melting point, 182·5–183·0°, $[\alpha]_D^{25} = -21\cdot7°$ (*c*, 3·0 in chloroform) ; analytical calculation for $C_{40}H_{54}O_{27}$: C 49·69, H 5·63 per cent ; found : C 49·65, H 5·86 per cent. Adding the molecular rotation of laminaribiose and the molecular rotational increment in the series of cellodextrins gives + 12·1°, which is in good agreement with $[\alpha]_D = +10°$ of our trisaccharide. Prof. S. Peat and his co-workers[6], however, reported 3-O-β-cellobiosylglucose (β-acetate : melting point, 108–110°, $[\alpha]_D = -8\cdot3°$) in the partial acidic hydrolysate of lichenin.

Acidic hydrolysis of sugar *c* also gave only glucose. It was shown to be a tetrasaccharide by the method described above. After partial acidic hydrolysis laminaribiose, cellobiose and trisaccharide mixture were detected, in addition to glucose and parent sugar. Consequently, it was inferred that sugar *c* was a tetrasaccharide containing at least one β-1 : 3- and one β-1 : 4-linkage.

The amylo process with starch materials other than barley showed 94–96 per cent sugar consumption and did not leave the above β-linked glucosyl oligosaccharides in such amount as is detectable on paper chromatogram. Further, the amount of these oligosaccharides isolated from the fermented barley mash was sufficiently large to preclude the possibility of their being products of transglucosidation by amylo moulds, since their power of transglucosidation is known to be extremely weak[7]. Furthermore, the main products of acid reversion of glucose include 1 : 6-linked disaccharides[8] and lævoglucosan[9]. In the actual experiment, no lævoglucosan was detected and only infinitesimal amounts of 1 : 6-linked sugars (*iso*maltose or gentiobiose) were isolated. Recently, R. A. Aitken *et al.*[10] detected laminaribiose and cellobiose in the enzymatic hydrolysate of barley glucosan. G. C. Aspinall and R. G. J. Telfer[11], who also studied the methylation of barley glucosans, indicated the presence of a polysaccharide containing unbranched chains of β-D-glucopyranose residues with approximately equal proportions of 1 : 3- and 1 : 4-linkages. From these facts, our β-linked glucosyl oligosaccharides are thought to be derived from the fragmentation of a β-glucosan.

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Selective Inhibition of Formation of Deoxyribonucleic Acid in *Escherichia coli* by Mitomycin *C*

Previous studies with mitomycin *C*, a new antibiotic isolated from *Streptomyces caespitosus* by Wakaki *et al.*, have demonstrated antibacterial activity as well as a marked antitumour effect[1,2]. In the course of investigating the mechanism of the actions of mitomycin *C*, evidence was obtained that this antibiotic selectively inhibits the synthesis of deoxyribonucleic acid in *Escherichia coli B*.

Cells grown in a salts–glucose synthetic medium were harvested during the logarithmic phase, washed and resuspended in a similar fresh medium with or without mitomycin *C*, to give a concentration of 1×10^8 cells per ml. 20 ml. of the bacterial suspension were incubated at 35° with shaking, and aliquots of 2 ml. were taken at the intervals shown, and analysed for turbidity, nucleic acid and protein. Turbidity was measured photometrically at 660 mμ and viability of the cells was measured by plating. Ribonucleic and deoxyribonucleic acid were assayed by the orcinol and diphenylamine methods respectively, after extraction from the acid-insoluble precipitates of bacteria with hot 6 per cent perchloric acid. The protein content was measured by the Folin method.

Table 1. EFFECT OF MITOMYCIN *C* ON THE GROWTH, PROTEIN AND NUCLEIC ACID SYNTHESIS OF *E. coli* B

Mitomycin *C* in suspension (μgm./ml.)	Time incubated (min.)	Turbidity E_{660}	Protein (Folin reaction) E_{660}	Ribonucleic acid (orcinol reaction) E_{660}	Deoxyribonucleic acid (diphenylamine reaction) E_{600}
0	0	0·090	0·070	0·110	0·030
	30	0·125	0·105	0·160	0·045
	60	0·180	0·150	0·225	0·065
	90	0·265	0·210	0·315	0·090
0·1	0	0·090	0·065	0·110	0·030
	30	0·135	0·100	0·155	0·030
	60	0·185	0·140	0·230	0·030
	90	0·225	0·190	0·320	0·030

Alterations in the bacteria during exposure to 0·1 μgm./ml. of mitomycin *C* are illustrated in Table 1. A normal increase in turbidity was observed during the first 60 min., after which the rate of increase in turbidity slowed down. However, after 90 min. of incubation there were only 1×10^6 viable cells/ml. as measured by plate count. Deoxyribonucleic acid formation was completely inhibited by the presence of mitomycin *C*, although synthesis of protein and ribonucleic acid was unaffected as compared with that of an unexposed culture during the test period. The inhibition of synthesis of deoxyribonucleic acid in the presence of the antibiotic could be reduced to some extent by the addition of baker's yeast extract to the incubation medium. The inhibitory action of mitomycin *C* on synthesis of deoxyribonucleic acid was observed even after removing the cells from mitomycin *C* and washing with saline.

Experiments on the effects of this compound on synthesis of deoxyribonucleic acid with the purified Kornberg enzyme are now in progress in an attempt to clarify the exact mechanism of the inhibitory action. A more detailed report will be published elsewhere.

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ANIMAL PHYSIOLOGY

Biosynthesis of Ovalbumin

THE problem of the biosynthesis of ovalbumin is interesting since this protein seems to be synthesized from a non-homogeneous pool of intermediary peptides[1-3]. We have studied the biosynthesis of this protein *in vivo* by the laying hen using L-cystine-^{35}S and $Na_2{}^{14}CO_3$. Selected birds were given these labelled substances and blood was obtained at stated intervals, either by heart puncture or from the wing vein. The time of laying the egg was carefully noted and ovalbumin was isolated from the egg white by ammonium sulphate fractionation. Serum globulin was isolated by precipitation with an equal volume of ammonium sulphate, while the total proteins were obtained by precipitation with trichloracetic acid to a final concentration of 5 per cent. In both cases the precipitates were repeatedly washed with 5 per cent trichloracetic acid to remove any co-precipitated amino-acids.

The results shown in Tables 1 and 2 indicate that the ovalbumin of eggs laid within 24 hr. of administration of the isotope was not significantly radioactive. The radioactivity of the ovalbumin is not high when that of the serum amino-acids is high. But the ovalbumin from eggs laid after 30 hr., when the radioactivity is found in the serum proteins and not in the serum amino-acids, is markedly radioactive. This shows that ovalbumin is not synthesized by the oviduct from the serum amino-acid pool, but probably from derivatives of serum proteins or intermediary peptide pools. The mechanism of the biosynthesis of ovalbumin is thus different from that of milk proteins, which have been shown to be derived from serum amino-acids[4].

Table 1. INCORPORATION OF CARBON-14 DIOXIDE INTO SERUM AND EGG PROTEIN

Bird No.	Time from administration of $^{14}CO_2$	C.p.m./ml. of serum, non-protein part	C.p.m./mgm. total serum proteins	Time of laying the egg from time isotope was given (hr.)	C.p.m./mgm. of ovalbumin isolated
1	17	2,000	19·8	44	104
	25	800	30·6		
	45	600	29·0		
2	8	3,300	237	22	nil
	25	1,930	230		
	45	400	266		

It could be argued that the oviduct might store serum amino-acids as a reserve and utilize them after 24 hr. That such storage of free amino-acids is not the case seems to be indicated by the following facts: (1) boiled juice from the oviduct has a very small content of free amino-acids as shown by the ninhydrin test; and (2) ovalbumin from eggs obtained as much as 48 hr. after the administration of the isotope is still radioactive. By this time the serum amino-acids have lost a considerable part of their radioactivity. It is difficult to appreciate that the amino-acids stored in the oviduct are not in equilibrium (even with a low exchange) with those in the serum.

However, such storage of a polypeptide precursor in the oviduct is not improbable, because our *in vitro* studies (Table 3) seem to indicate that the synthesis of ovalbumin by washed oviduct preparations is fairly independent of added amino-acids, adenosine triphosphate, etc. The amount of ovalbumin syn-

Table 2. INCORPORATION OF CYSTINE-^{35}S INTO PROTEINS

Bird No.	Hr. after administration of cystine-^{35}S	Non-protein radioactivity c.p.m./ml. serum	C.p.m./mgm. of total serum protein	C.p.m./mgm. of globulin fraction	Time of laying egg from time isotope was given (hr.)	C.p.m./mgm. ovalbumin isotope	C.p.m./mgm. yolk protein
3	3	800		29·4			
	20	350	25·4	24·3	22	1·0	Nil
	49	Nil		52·0	49*	79·9	3·8
4	3	1,600	56·6	36·9			
	20	800	33·3	42·9	35	52·6	8·0
	49	Nil	35·7	34·1	49*	38·7	9·6

* The egg was obtained from the oviduct when the hens were killed.

Table 3. *In vitro* SYNTHESIS OF OVALBUMIN BY OVIDUCT SLICES

Time of incubation (hr.)	Ovalbumin synthesized (μgm. per ml. of incubate)		
	Slices alone	Slices+amino-acids+ ATP+FDP	Slices+amino-acids+ ATP+FDP+ hydroxylamine
1½	308	268	268
3	408	418	348
5	504	418	348

ATP, Adenosine triphosphate; FDP, fructose-1,6-diphosphate.

thesized in the *in vitro* incubation of oviduct with a complete medium, or in the absence of any additions, was estimated by antigen analysis techniques using rabbit anti-hen egg albumin sera. These sera were standardized previously with pure ovalbumin. These results show that the oviduct can synthesize ovalbumin without any further additions, and also that hydroxylamine does not have strong inhibitory action on this synthesis. This may possibly suggest a conversion of an ovalbumin precursor to ovalbumin not dependent on added adenosine triphosphate.

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Molecular Orientation at the Surface of *Amoebae* during Pinocytosis

PINOCYTOSIS[1] or cell-drinking appears to be a method for the uptake of molecules to which the cell membrane is impermeable[2]. In *Amoebae* the phenomenon may be identified by the formation of many short pseudopods each containing a central channel 1μ or more in diameter; droplets of fluid pinch off from this channel and migrate into the interior of the cell[3]. Recently, pinocytosis has become the subject of considerable physiological experimentation[2,4–6]. By means of fluorescein-labelled proteins, Brandt[5] demonstrated that proteins inducing pinocytosis are attached to the cell membrane of *Amoebae*. Schumaker[6] obtained results on the rate of uptake of radioactive proteins which lead to a similar conclusion.

In order to speculate intelligently about the induction of pinocytosis it would be of interest to know more about this attachment. Some information can be obtained from polarization microscopy, which will reveal the molecular orientation of the cell membrane and, in certain instances, of substances attached to the surface. The present preliminary communication describes interactions between pinocytosis-inducers and the surface of *Amoeba proteus* determined by the use of the polarizing microscope.

Mitchison[7] confirmed the well-known natural surface birefringence of *Amoebae* and showed that various basic dyes are oriented at the surface in an orderly molecular array *in vivo*. The surface orientation of these anomalously birefringent basic dyes may be shown by the striking differences in colour (for example, blue versus yellow) that appear when the surface faces different quadrants of the compensated polarizing microscope.

The first experiments were simple comparisons of cells in their inorganic culture medium and cells pinocytosing in either albumin or ribonuclease. There were no qualitative differences in the surface birefringence of the cells in the different media. The surfaces of the pinocytosis channels also showed the same molecular orientation as the rest of the cell surface (Fig. 1*a* and *b*). Hence, it may be concluded that there is no major re-arrangement of the orientation of molecules in the cell membrane. Quantitative studies of possible small differences do not appear to be feasible, because the errors in measurement[8] would vary as the square of the inaccuracy in determining the diameters of both the narrow channel and the wider pseudopod.

In the course of repeating Mitchison's experiments on the surface orientation of anomolously birefringent basic dyes[7], it was found that at higher concentrations toluidine blue not only became attached to the surface of *Amoebae* in a definite molecular orientation but also induced pinocytosis. There were no qualitative differences in dye orientation between the channels and other parts of the cell.

Two types of qualitative changes that have been described previously by Mitchison were seen in random parts of some cells. The first was the loss of dye-binding capacity but not natural birefringence accompanying surface 'bubbling'. The second was a 90° change in the orientation of the dye molecules with respect to the visible edge of the cell as evidenced by a colour change.

When the cells were first placed in dye solutions there were often strong differences in colour intensity between different parts of the surface of the same cell. Sometimes these differences could be discerned as absorption differences with transmitted (unpolarized) light. The increase in intensity could be watched on parts of cells which did not change shape. These observations indicate both local surface differences in the number of available dye-binding sites and a time-dependent attachment.

In order to test the hypothesis that proteins might also be absorbed to the same specific surface groups

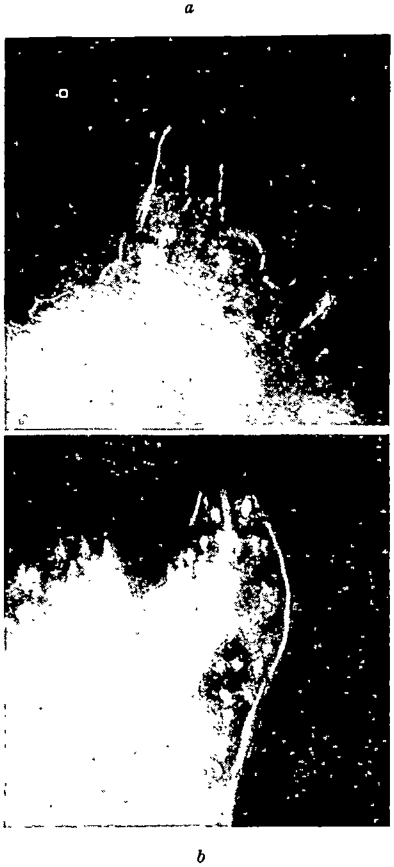

Fig. 1

during the induction of pinocytosis, a series of experiments was performed using both proteins and toluidine blue. Three designs were employed: simple competition with both pinocytosis-inducers present, addition of the dye to a protein solution containing pinocytosing *Amoebae*, and addition of protein to a dye solution containing pinocytosing cells. Four proteins were tested separately: albumin, protamine, ribonuclease, and trypsin. In all instances there was competition dependent on concentration between the dye and the protein for surface sites as evidenced by the comparison of natural surface birefringence with the anomalous birefringence colours of the attached dye. Ribonuclease and protamine, two basic proteins, appeared to be more effective than either albumin or trypsin; however, the relative effectiveness will require further examination under conditions of varying *p*H and salt concentration.

The competition experiments suggest that proteins are not only attached to the cell surface[5,6] but also that they are attached in an orderly molecular array. Since only basic dyes are oriented at the cell surface[7] and the basic proteins appear to compete most favourably with these dyes, it is also reasonable to postulate that the sites on the cell surface are acidic.

This method, while indirect, is highly sensitive, and should prove to be a valuable tool for the further study of surface interactions in the induction and inhibition of pinocytosis.

This work was performed during the tenure of a research fellowship of the National Cancer Institute of the U.S. Public Health Service. I wish to thank Dr. J. M. Mitchison not only for instruction in the techniques of precision polarization microscopy but also for suggesting re-examination of the dye orientation. I am also grateful to Dr. Mitchison, Prof. M. M. Swann, Dr. N. de Terra, and Prof. H. Holter for stimulating discussions about these problems.

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Re-utilization of Lymphocyte Remnants by Reticular Cells

The behaviour and function of lymphocytes were discussed at a meeting in London in 1957[1]. As a consequence of the results of experiments with radioactive labels[2], the hypothesis of continuous re-utilization of large fragments of lymphocyte nucleic acids or nucleoproteins during the formation of new lymphocytes was generally accepted. Morphological support for this view has been put forward by Trowell[3], who has demonstrated that the reticular cells are differentiated into large lymphocytes in the course of phagocytosis of dead lymphocytes *in vitro*. We have been able to supplement his findings by similar observations made during the time of heightened lymphocyte dissolution *in vivo*.

I have studied the experimentally elicited disintegration of lymphocytes in spleen lymphatic nodules. The mice of *H*-strain were subjected to total-body irradiation of 500 r., 650 r., and 750 r.; rats of the Wistar strain were subjected to formaldehyde stress and normal and adrenalectomized ones to hydrocortisone ('Scheroson *F*' Shering, 4 mgm./100 gm. body-weight). X-rays were delivered at the rate of 45 r./min. (180 kV., 15 m.amp., filters 1 mm. aluminium and 0·5 mm. copper, target distance 55 cm.). The spleens were fixed in Helly–Maximow's fluid and dyed by azur II – eosin, methyl green – pyronin and by the Feulgen nuclear reaction. The specificity of ribonucleic acid staining by pyronin was controlled by means of the perchloric acid extraction technique.

In the course of dissolution of the lymphocytes, the cytoplasm of reticular cells became deeply basophilic. At the same time their nuclei and nucleoli enlarged. The strikingly close association of lymphocyte dissolution with transformation of reticular cells was seen under the following conditions.

The formaldehyde injection may elicit a stress disintegration of lymphocytes in light centres and a marked swelling of lymphoid tissue of spleen lymphatic nodules[4]. At 6 hr. after the injection, extensive masses of large immature lymphoid cells are formed at the periphery of centres. They originate in the reticular cells occupying the corresponding part of light centres in non-stressed rats. Quite similar events are observed after the injection of hydrocortisone in adrenalectomized rats. A pronounced swelling of lymphoid tissue and disintegration of lymphocytes in the centres of the nodules occur within 3 hr. At 6 hr., groups of immature cells having large nuclei and intensive pyroninophilic cytoplasm develop. In normal rats treated by hydrocortisone, however, both the disintegration of lymphocytes and swelling of lymphoid tissue are negligible, and the immature cells fail to be differentiated.

In comparison with stress, the transformation of reticular cells is shown more clearly in a denuded reticular network of spleen lymphoid tissue of an irradiated animal. Most lymphocytes undergo disintegration and fill the spaces of the reticular stroma with numerous fragments. No phagocytosis takes place. The reticular cells adjacent to fragments show a gradual rise in cytoplasmic basophilia and the nuclei and nucleoli become enlarged as in immature cells. During this change they differ essentially from those originally building up the nodule reticulum. In the transition stages a pyronin-staining reaction may be seen around the nucleus, leaving the rest of the cytoplasm and the cytoplasmic processes almost unstained. The incidence and/or intensity of pyroninophilia of reticular cells seem to depend upon integrity of a humoral union with red pulp, in addition to an abundance of lymphocyte remnants. The pyroninophilia appears to be more intense at the periphery of the nodules than in destroyed light centres, separated from the red pulp by a dense reticular envelope. Swelling of the lymphoid tissue accompanies both the dissolution of lymphocytes and the increasing reticular pyroninophilia, as it does in the case of unspecific stress.

Eventually, the enlarged pyroninophilic reticular cells develop into more differentiated ones, mainly into immature plasma cells, but a few form large and medium-sized lymphocytes. Immature plasma cells originating in this way may occupy extensive areas of destroyed lymphoid tissue from as soon as 12 hr. after irradiation.

In mice irradiated with lethal doses of 650 r. or 750 r., and so deprived of most of their lymphocytes, the reverse 'differentiation' can be observed. At the time of disappearance of lymphocyte debris the large groups of immature cells may survive in the nodules. However, the basophilia of their cytoplasm begins to diminish until it disappears in 24–48 hr. after the irradiation. The immature cell groups undergo a dedifferentiation into a voluminous cytoplasmic syncytial mass which is not stained with pyronin. The large vesicular nuclei, in their persistence at the time of loss of pyronin stainability and of cell coupling into a syncytial feature, are proof that dedifferentiation has occurred.

These observations indicate the close relation between the dissolution of lymphocytes and the transformation of resting reticular cells into cell elements with a high power of differentiation, in accordance with the apparent signs of immaturity. The intimate local and temporal coincidence of both the dissolution of lymphocytes and the transformation of reticular cells are striking. In addition, the reverse, that is, the dedifferentiation, can also be found. The striking incidence of numerous cell fragments in proliferating centres of lymphatic nodules is stressed by DeBruyn[5] and by Ringertz and Adamson[6]. Furthermore, Dougherty and White[7] describe both dissolution of lymphocytes and an increased number of immature plasma cells as the result of adrenocortical stimulation.

These observations and results recorded in the literature suggest that dissolution of lymphocytes produces a humoral factor—probably a derivative of their nucleic acids or nucleoproteins—with the ability to maintain the cytological characteristics of immature cells on the normal level, in participating in their nucleic acid metabolism. Raising the production of such a factor in the course of heightened lymphocyte dissolution, new resting cells become transformed into immature ones; decreasing production in the case of lymphocyte deprivation, a dedifferentiation of immature cells into reticular ones occurs.

Further details of this work will be published elsewhere.

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A Survival Curve for Mammalian Cells irradiated *in vivo*

HIGH density single-cell suspensions of transplantable mouse leukæmia cells have been prepared from the infiltrated livers of leukæmic *CBA* mice. The density of morphologically healthy malignant cells in a suspension was determined by counting by phase-contrast microscopy, and selected serial dilutions of the counted suspension were injected intraperitoneally into groups of isologous mice. From the leukæmia mortalities in the injected groups the mean number of leukæmia cells required to convey leukæmia to half a group of injected mice (the *TD*50) was calculated by the method of Reed and Muench[1]. In six such bio-assays of suspensions from the livers of untreated leukæmic mice, *TD*50 values ranging from 0·7 to 3·0 (mean 2·0) were obtained.

The densities of morphologically intact leukæmia cells in suspensions prepared from the livers of leukæmic mice within a few minutes of the end of their exposure *in vivo* to cobalt-60 gamma whole-body radiation, delivered at a dose-rate of about 75 r./min., were found not to have been influenced by the preliminary irradiation of the mice. Bio-assays of suspensions from such irradiated mice, however, gave *TD*50 values which were raised above the mean *TD*50 (2·0 cells) obtained for suspensions from unirradiated leukæmic mice and which were a function of the radiation dose. This is to say that a proportion of the exposed leukæmic cells were found to have lost their reproductive integrity soon after irradiation without having sustained visible damage.

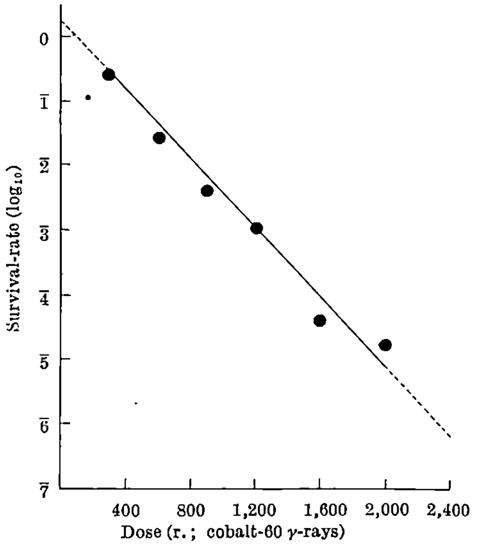

Fig. 1. Variation of log survival-rate and radiation dose for *CBA* leukæmia cells irradiated *in vivo*

The log survival-rate among the leukæmia cells from an irradiated mouse was calculated simply by subtracting the log of the *TD*50 given by the cells from the irradiated mouse from the log of the mean *TD*50 (2 cells) obtained for cells from unirradiated mice. A series of six log survival-rates was determined for cells from individual leukæmic mice which had received whole-body radiation doses between 300 r. and 2,000 r. Within the limits of experimental error, a linear relationship was demonstrated between radiation dose and log survival-rate (Fig. 1).

The curve, drawn by inspection through the points obtained by experiment, indicates a D_0 value (dose of radiation required to reduce the reproductively intact leukæmia cells to 37 per cent) of 162 r. The curve has been confirmed by a series of six further determinations of survival-rates for radiation doses within the range used initially.

In more recent experiments we have shown that the survival-rate for leukæmia cells irradiated *in vivo* in mice breathing 95 per cent oxygen was similar to that for cells from mice breathing 20 per cent oxygen during irradiation. The survival curve for cells irradiated in mice immediately after death, however, under which conditions the cells are assumed to be in an anoxic environment, showed that the anoxic cells were relatively resistant to radiation, approximately 2·3 times the dose of radiation being required for equal survival-rates.

The linear log survival curve obtained for HeLa cells irradiated *in vitro* by Puck and Marcus[3] gave a D_0 value of 96 r. for 230 kV. X-radiation. The D_0 value for leukæmia cells irradiated *in vivo*, after multiplication by the factor 0·75 to allow for the relative biological effectiveness of cobalt-60 gamma-rays compared with 230 kV. X-rays, is 122 r. The comparison indicates that the human cancer cells irradiated *in vitro* are more sensitive to radiation than the mouse leukæmia cells irradiated *in vivo*. However, incomplete studies by us have suggested that the radiosensitivity of mouse leukæmia cells irradiated *in vitro* may approach that of HeLa cells irradiated *in vitro*. The differences observed between the human and mouse cells may, therefore, prove to be due to the different conditions of the cells during irradiation rather than to the difference of species.

The work described is to be reported in detail elsewhere.

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Relative Rates of Liver Storage of Pure α-, β-, γ- and δ-Tocopherols in the Growing Chick

Previous work in this laboratory on the storage of vitamin E in growing chicks has shown that only α-tocopherol was present in the liver. Since normal poultry foods often contain a high proportion of non-α-tocopherols[1,2] the ability of the chick to utilize these compounds is of importance. American workers, using the transfer of tocopherol into the egg as an index of utilization[3], found no evidence of the conversion of either γ- or δ-tocopherol to α-tocopherol, but direct measurements of liver storage were not made.

Groups of six birds of a commercial broiler strain (New Hampshire Light Sussex × White Rock) aged six weeks were placed on a purified diet low in vitamin E and depleted for a period of three weeks. Then over a period of five days they were given a series of oral doses of pure α-, β-, γ- or δ-tocopherol in ethanol–water emulsion. Two days after the final dose the birds were killed.

Blood samples were taken and whole livers were removed for tocopherol assay. Lipids were extracted using a modified form of the procedure of Swick and Baumann[4]. Saponification and removal of sterols, carotenoids and vitamin A were carried out using Brown's methods[5], and finally individual tocopherols were separated and identified by means of the two-dimensional paper chromatographic procedure of Green[2].

It was not found possible to identify any individual tocopherol in blood; but all tocopherols were found in liver with the exception of δ-tocopherol. Relative concentrations and recovery rates are given in Table 1.

The relative biological activities for α-, β-, γ- and δ-tocopherols have been quoted by Brown[5] as 100 : 30 : 20 : 1, and Ames[6] as 100 : 6 : 1 : 1 and later[7] as 100 : 33 : 1 : <1. The relative rates of liver storage quoted in Table 1 show some correlation with these values and might offer some explanation for the lower biological activities of non-α-tocopherols and especially of δ-tocopherol.

However, an additional factor in the consideration of biological activity in natural products is that of

Table 1

	Total dose 6 birds (mgm.)	Concentration found in fresh liver (μgm./gm.)	Total recovered in livers (mgm.)	Relative percentage recovery ($\alpha = 100$)
α-Tocopherol	120	1·90 ± 0·19	0·289	100
β-Tocopherol	100	0·76 ± 0·17	0·099	41·2
γ-Tocopherol	120	0·34 ± 0·15	0·054	18·7
δ-Tocopherol	100	Nil	Nil	Nil

availability. Bunnell[8] has shown that the availability of α-tocopherol in lucerne to be only about 30 per cent.

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Normal Components of Guinea Pig Serum which may cause Antigens to show an Apparent Anti-complementary Effect

Normal guinea pig serum is the most common source of complement for the complement-fixation test, and may be used fresh or, more commonly, preserved either by freeze-drying or by Richardson's method[1]. Such 'complement' is used in the presence of a great variety of antigens, and the possibility of a reaction between components of this serum other than complement and the antigen is usually either ignored or allowed for as an anti-complementary effect of the antigen acting alone.

To investigate such reactions, normal guinea pig serum was obtained by cardiac puncture from thirty animals, pooled, and preserved by Richardson's method. Following titration this serum was diluted with barbitone buffer solution, so as to contain 12·5 *MHD*50 units (minimal hæmolytic dose giving 50 per cent hæmolysis) per unit volume of 0·5 ml.

1 mgm. 'Zymosan' (Fleischmann Laboratories, Stamford, Conn., U.S.A.)[2] was added to each of two aliquots of 2 ml. of this standardized serum, and these, together with two untreated aliquots, were then incubated at 17° C. for 30 min. One of the aliquots that had been treated with 'Zymosan' was then centrifuged at 3,000 r.p.m. for 3 min. at 0° C. The supernatant fluid was decanted off and recentrifuged to ensure that all traces of the 'Zymosan' had been removed. To the final supernatant fluid 0·5 ml. barbitone buffer solution and a further 1 mgm. 'Zymosan' were added. 0·5 ml. of a 1 : 15 solution of Wassermann antigen (Burroughs Wellcome, alcoholic extract of sheep heart with cholesterol) in barbitone buffer solution was added to one of the aliquots that had not previously been treated with 'Zymosan', and also 0·5 ml. of the barbitone buffer solution to the remaining two aliquots. All four aliquots were then incubated at 37° C. for 15 min.

The amount of complement remaining after the various treatments was determined by titration. The technique used for this titration involved a serial dilution of the four solutions containing the residual complement, with a log dilution factor of 0·125. When 0·5 ml. amounts of each dilution were incubated at 37° C. for 60 min. with 2 ml. of a 0·5 per cent suspension of sheep red cells optimally sensitized with anti-sheep red cell hæmolysin (Burroughs Wellcome), several tubes were obtained within the zone of partial hæmolysis. The degree of hæmolysis in each tube of the titration was estimated by means of an EEL portable colorimeter, and the titre calculated graphically[3].

Pillemer and his co-workers have demonstrated that normal guinea pig serum contains 'Properdin'[4], and this has been shown to combine with components of preparations from a very great variety of plant and animal sources, for example, yeasts ('Zymosan'), bacteria, inulin, dextrans, gastric mucin, viruses, protozoa, trematodes, etc.[5-8]. When such preparations are used as antigens, the complexes so formed are capable of fixing complement by specifically inactivating the third component, at temperatures above 18° C. Below 18° C., however, although the complex is formed, it does not inactivate complement[4]. A factor which will fix complement in the presence of the Wassermann antigen is known to occur in the normal serum of many adult animals, although guinea pig serum has been reputed not to possess this property[9].

Table 1. The Percentage of the Initial Complement remaining following the Various Treatments

Treatment of guinea pig serum		Residual complement as percentage of initial complement (per cent)
Treated with 'Zymosan'	'Zymosan-Properdin' complex removed	46
	'Zymosan-Properdin' complex remains	23
Not treated with 'Zymosan'	Wassermann antigen added	21
	Wassermann antigen not added	63

The results presented in Table 1 show that the amount of complement fixed by the 'Properdin-Zymosan' complex, or by the Wassermann system was markedly greater than the loss of complement activity occurring during the process of incubation, or due to the presence of 'Zymosan' after most of the 'Properdin' has been removed. In the presence of an excess of antigen, this activity will vary with the amount of guinea pig serum present, independently of its complement content, unlike a true anti-complementary effect. Any allowance to be made for this effect, in addition to that made for any anti-complementary action of the antigen, must therefore be determined using the same amount of guinea pig serum as is to be used to provide the complement for the fixation tests in question.

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Audio-direction Finding in the Porpoise (*Phocaena phocaena*)

The excellent anatomical work by Reysenbach de Haan[1], the important work on *Tursiops* by Scheville *et al.*[2], and numerous field observations have shown that cetaceans hear extremely well. *Tursiops* appears to possess a sonar system of remarkable quality[3] and one is inclined to believe that such a system may be of general occurrence[4], at any event among the toothed whales.

One of the striking features of hearing in the animal kingdom is the perception of the direction of sound. Experiments with man have shown that the accuracy of perception of direction is based on the difference in time the sound needs to reach both ears. In the case of pure tones and continuous tones the case is somewhat more complicated, phase differences playing a major part at lower frequencies up to about 2,000 c./s., whereas at higher frequencies differences of intensity are of special importance.

Sedee[5] has shown that in man the accuracy with which the direction of sound is determined depends, first, on the angle between this direction and the sagittal plane of the head, and, secondly, on the distance between the ears. Using an artificial head twice as large as normal, he found the threshold angle of direction to be about half its normal value.

Since sound waves travel faster in water than in air, and since the working distance between the bullæ in the porpoise is smaller than that in man, the question arises whether at lower frequencies—where differences of intensity do not play a predominant part—discrimination of direction in cetaceans may be less accurate than that in man, owing to the smaller time-differences involved. In order to get some insight into the matter, experiments were made with a porpoise.

A male porpoise was trained to come to the vicinity of the source of a sound signal by rewarding it with a fish. The underwater signal was produced by a Philips commercial tone-generator and emitted by two barium titanate transducers, one at a time. The transducers were placed at varying distances from each other and the signal was a pure tone, click-free and of short duration (± ⅔ sec.). The signal was given when the animal was on a marked spot at about 18 m. from both transducers. The porpoise could only reach the vicinity of a transducer—which were separated from one another by a net—through a corridor about 12 m. long, and the animal had to choose the right opening at that distance. The enclosure in which the animal was kept had muddy slopes and eel grass on its bottom. It was therefore practically free from disturbing echoes.

It was found that the porpoise chose the right corridor if the mean angle between the transducers—one on the left side and one on the right side of the sagittal plane in front of the animal—was at least 16°. This was when a tone of 6,000 c./s. was used; at 3,500 c./s. the minimum angle is less narrow, at least 22°.

It appears from unpublished observations of Sedee, especially made on our behalf, that in man, when using the same kind of signal (but in the air), the angle in question is about 16° at 1,500 c./s. (giving the same wave-length as 6,000 c./s. in water) and about 24° at 750 c./s. The narrowest angle obtained at 1,500 c./s. was 8–10°, however, apparently half the width of that in the porpoise. As the distance between the bullæ tympani of a porpoise is about half the distance between the ears of man, it appears that, roughly speaking, a porpoise in water and a man in air have about the same degree of acuity of perception of the direction of sound when similar wave-lengths are compared.

Financial and other aid making this investigation possible was obtained from the Netherlands Organization of Pure Research (Z.W.O.), the Laboratory for Comparative Physiology at Utrecht, the Zoological Laboratory of the University of Amsterdam, the Linnaeus Fund, Amsterdam, the Verenigde Toeristen Bedrijven at Harderwijk, the Texel Museum Foundation and several Danish friends. Special thanks are due to Dr. G. A. Sedee, Utrecht, and to Mr. G. J. de Haan, Texel.

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PLANT PHYSIOLOGY

Effect of Light on Maturing Broad Bean Seeds

We have recently shown[1] that the typical development of the etiolated broad bean shoot in darkness is modified by exposing the intact soaked seed to light and that the sensitivity develops at the time when the embryo takes up water. It was suggested that the embryo of the maturing seed may also be sensitive in the same way and that varying conditions of light during maturation may affect the subsequent development of the seedling.

The following experiment was carried out to test whether a light effect on the maturing embryo could be detected in seedlings grown in darkness. Plants were raised in natural light conditions, and some of the pods were enclosed in light-tight bags at an early stage when they were approximately 1 in. long. When mature the seeds were removed from the pods and dried in complete darkness. Seeds from uncovered pods were simultaneously dried in the light for the same period. All seeds were then germinated and grown in darkness; internode-lengths were measured after 13 days.

The mean length of the first internode from seeds matured in darkness (30 seedlings) turned out to be approximately 16 per cent greater than that from the controls (35 seedlings). This difference is significant at the $P = 0{\cdot}05$ level. Clearly the sensitivity develops during the maturation of the seed, and the effect survives a short drying process. The effect of light thus bears some resemblance to the vernalization effect on the embryo of winter rye in that treatment is effective *in the maturing embryo*[2]. The mean length of the first internode from seeds matured in the light does not differ significantly from that of controls grown in the dark from four previous experiments with commercially grown seeds (Table 1). It, in fact, lies above all the means from individual experiments.

Although the experiment was not designed to test this, the results suggest that the effect of light sur-

Table 1. MEAN LENGTH (CM.) OF FIRST INTERNODE OF SEEDLINGS GROWN IN DARKNESS FOR 13 DAYS INCLUDING THE PERIOD OF SOAKING

	Mean length (cm.) of first internode	
	A	*B*
Seeds matured in darkness	16·4 (0·837)	—
Seeds matured in light	14·16 (0·623)	13·13 (0·235)
Seeds exposed to 2 hr. light at 24 hr. after the beginning of soaking	—	10·47 (0·251)

Column *A* from the present experiment, column *B* from previous experiments with commercially grown seeds. Figures in brackets are standard errors of the means.

vives the normal long period of inactivity in stored seeds and that the first internode of etiolated seedlings is always partially suppressed by light. It may well be that the higher figure of our controls in the present experiment reflects a reaction to the lower light-intensity in which these seeds were matured as compared with the commercially grown seeds. We hope to verify these inferences by further experiment.

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Differential Reaction of Saprophytic and Parasitic Soil-inhabiting Fungi to Indoleacetic Acid

INDOLEACETIC acid was shown to be a product of fungus metabolism, when Thimann[1] in 1935 demonstrated that this was the growth-promoting substance (for higher plants) produced by cultures of *Rhizopus suinus*. Later, attempts to reproduce in fungi the growth responses to indoleacetic acid found in higher plants were not successful[2], and interest in this field has been limited. The importance of indoleacetic acid in fungus metabolism has, however, been emphasized by several recent reports, particularly of studies of host–parasite relationships[3–6].

In the course of experiments on the effects of indoleacetic acid on two saprophytic and two plant parasitic soil-inhabiting fungi, growth of the latter was found to be much more readily inhibited than that of the former. *Ophiobolus graminis* Sacc., which causes the well-known 'take-all' disease of wheat and other Gramineae, and *Fomes annosus* Fries, which is a common cause of root and heart rot of conifers, were the two parasites studied. The saprophytes were the two soil fungi *Trichoderma viride* Pers. ex Fries, and *Trichocladium asperum* Harz.

Indoleacetic acid at various concentrations was incorporated in a synthetic liquid medium at *p*H 5·5. The medium was dispensed in 25-ml. aliquots in 200-ml. Erlenmeyer flasks. A mycelium homogenate in 0·25 *M* sodium chloride was used for inoculating the flasks and growth was measured by determining the weight of dried mycelium which developed. Typical data are given in Table 1.

Table 1. EFFECT OF INDOLEACETIC ACID (IAA) ON GROWTH OF FOUR FUNGI

IAA × 10^{-5} *M*	Dry mycelium (mgm.)			
	T. viride	*T. asperum*	*O. graminis*	*F. annosus*
0	180·9	183·7	258·4	84·6
1·0	—	180·0	224·0	46·6
10·0	—	185·5	136·5	0
50·0	169·8	203·8	0	0
100·0	188·1	183·4	0	0
L.S.D. at 1 per cent	—	—	50·4	29·1

Neither *T. viride* nor *T. asperum* was significantly inhibited by concentrations of indoleacetic acid up to 100 × 10^{-5} *M*, while *O. graminis* and *F. annosus* were significantly inhibited at concentrations of 10 and 1 × 10^{-5} *M* respectively and were completely inhibited at higher concentrations. A number of unidentified saprophytic soil fungi behaved similarly to *T. viride* and *T. asperum* in that the higher concentrations of indoleacetic acid did not significantly reduce growth.

These results may have significance for the parasitic or saprophytic development of these fungi. An extension of these findings will be published elsewhere.

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Formation of Purple Pigment in *Spirogyra pratensis* Cultures

RECENTLY, investigation of the purple vacuolar pigment of *Zygogonium ericetorum* Kütz.[1] has disclosed that it is formed by an association of ferric ions with a gallo-tannin. Similar algal pigments reported as anthocyanin-like[2] or phycoporphyrin[3] by previous investigators are probably closely related or identical to the iron-tannin of *Zygogonium*.

Most of the algal species which produce purple cell sap are found in bogs or swamps where iron is more likely to be available in rather high concentration. In addition to *Zygogonium*, several other members of the Zygnemataceae produce tannin, and tannin production by *Spirogyra* has been studied[4]. Thus it is possible that other species, not reported to form purple pigment in Nature, might form pigment under appropriate cultural conditions.

In the course of studies of *Spirogyra pratensis* Transeau, one of us (A. A.) observed that, in Waris medium containing iron sequestrene, sub-cultures of the alga in which conjugation was occurring produced purple filaments. Similar sub-cultures in soil-water remained pale green. Although extensive tests were not conducted, the distinctive responses to ammonia and to hydrochloric acid[1] indicated that the pigment which developed in the sub-cultures in Waris medium was similar to that of *Zygogonium ericetorum*.

Afterwards, vegetative filaments of *Spirogyra pratensis* were transferred into flasks of soil-water and of Waris medium. Transfers were made also into small quantitites of soil-water and of Waris medium in watch glasses enclosed within deep Petri dishes. The latter were for the purpose of encouraging conjugation so that we might compare pigment production by sexual and vegetative material. The cultures were kept constantly at about 20° C. under cool white fluorescent lights on a 16-hr. photo-period.

The observations described here were made 35 days later. Material in flasks of soil-water was bright green while that in the flasks of Waris medium showed large patches of purple filaments among green filaments. In the watch glasses filaments in soil-water were pale yellow-green while those in the Waris medium were purple.

Filaments from the Waris medium were examined microscopically. Material in flasks of Waris medium, as well as that in watch glasses of Waris medium, showed some incipient and unsuccessfully completed conjugation. The filaments with purple pigment did not appear to be in a normal physiological state. The chromatophores were still green, but they did not have the regular spiral form typical of healthy cells. The cells were not readily plasmolysed, and the location of the pigment was in doubt. It may have been in the cell sap or perhaps adsorbed to the cell wall. There was no significant difference in the quantity of pigment formed in the material growing in Waris medium in shallow watch glasses and in flasks. Inasmuch as material in watch glasses of soil-water conjugated but did not accumulate purple pigment, it appears that the development of the pigment was not merely correlated with the occurrence of conjugation.

Although we must conclude that it has not been demonstrated that normal healthy cells of *Spirogyra pratensis* form purple pigment, the fact that the alga is capable of forming a large amount of the iron-tannin pigment in certain circumstances is of significance.

It seems now to be indicated that distinction between the algae which form purple pigment and those which do not does not depend upon their ability to synthesize a unique chromagenic substance, but rather upon their ability to tolerate an ecological niche in which iron is available in sufficient quantity to interact with the chromagen or upon their ability to accumulate the iron. There must be differences among species in their ability to produce tannins, of course; but it is obvious that, in *Spirogyra pratensis*, lack of tannin was not the limiting factor.

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BIOLOGY

Dissociated Nystagmus in the Rabbit

A PROMINENT feature of all forms of nystagmus is the strict co-ordination of movement of both eyes, brought about by fibre systems which cross from one side to the other. We have observed a curious phenomenon in which both eyes move synchronously but in opposite directions.

A longitudinal channel was cut in the rabbit's skull, extending caudally from the coronary suture to the region of the inferior colliculus and running along the sagittal suture. When a fine knife was guided along this channel, at a depth of 10–12 mm. from the surface of the skull, a spontaneous nystagmus, starting with a slow adduction of both eyeballs, was observed in 60 per cent of our experiments. During the rapid phase, the right eye moved to the right and the left one to the left side, that is, simultaneous contraction of both external rectus muscles occurred. The rhythm of this nystagmus was slow and irregular, but exact synchronicity was always preserved, as shown in the nystagmogram (Fig. 1).

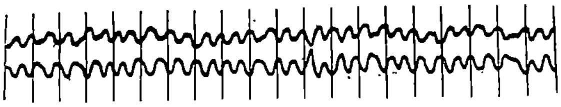

Fig. 1. Nystagmogram of dissociated nystagmus. Upper curve, left eye; lower curve, right eye. Excursions upwards indicate movement of eyeballs to right, downwards to left. Vertical lines, time (sec.). Note irregularity and synchronicity of the dissociated nystagmus

The dissociated nystagmus lasted only for a brief period (some seconds, up to several minutes). This suggests that the acute lesion was responsible for the phenomenon. Rotation of the rabbit during the spontaneous movements, or electrical stimulation of the 'nystagmogenic centre' in the midbrain[1] produced the normal response, which superseded the dissociated nystagmus. It is thus evident that cross-connexions between left and right are still available, although the decussation, occurring in the posterior commissure[2], has been divided. This conclusion is supported by the fact that application of deeper cuts abolishes the dissociated nystagmus as well as the response to labyrinthine or central stimulation.

A full description of these experiments will be published in the *American Journal of Physiology*.

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Strain Differentiation in a Root-infecting Fungus

IN various fields of mycology it has long been realized that, for certain purposes, the orthodox descriptive method of systematic classification is by no means adequate. Fungal strains grouped together on the bais of similar physiological reactions have been found to cut right across species of diverse taxonomic affinities, and it appears that in such disciplines as, for example, clinical medicine, agriculture, and forest pathology, the strain rather than the species is frequently of importance.

While studying the influence of certain root-infecting mycelia on the development of forest tree seedlings, unequal growth effects on the young plants were observed which strongly suggested different strains of the same fungal species as being responsible for the dissimilar performances of the seedlings. Confirmation of such strain differentiation was obtained

Table 1. Pure-Culture Reactions of Various Isolates of *Boletus scaber*

Origin of isolates of *B. scaber*	(*a*) Growth on litters	(*b*) Guaiac test	(*c*) Bavendamm test		(*d*) 'D.T.A.' medium		(*e*) Tryptophan medium	
			Growth	Reaction	Growth	Reaction	Growth	Reaction
(1) Heathland: Dorset	+	−	+	−	+	+	+	+
(2) Heathland: Surrey	+	−	+	−	+	−	(+)	−
(3) Moorland: Yorkshire	−	+	−		−		−	
(4) Woodland: Middlesex	−	+	−		−		−	
(5) Woodland: Berkshire	−	+	−		−		−	
(6) Woodland: Hertfordshire	−	+	−		−		−	
(7) Centraalbureau v. Schimmelcultures: Holland (ex Sweden)	−	+	−		−		−	

by pure culture tests of various isolates of the fungal species under observation. The species generally designated *Boletus scaber* Bull. (*Leccinum scabrum* S. F. Gray; *Krombholzia scabra* [Fr.] Karst.) was used as one of the main objects for these pure-culture tests, since two isolates of this fungus had been observed to influence the growth of young birch trees unequally[1]. Altogether, seven isolates of *B. scaber* were submitted to the tests. Two of the mycelia, (1) and (2), were derived from sporophores collected from heathland soils; another, (3), came from a sporophore on a moorland soil; (4), (5) and (6) were isolated (by M. E. Parry) from fruit-bodies of the species appearing in deciduous woods. The Centraalbureau voor Schimmelcultures in Baarn, Holland, kindly supplied isolate (7), ex Sweden.

These mycelia were tested along the following lines: (*a*) growth reactions on various broadleaf-, conifer-, and heather-litters (steam-sterilized); (*b*) gum guaiac test; (*c*) Bavendamm test (using 0·1–0·3 per cent tannic acid); (*d*) growth and colour reaction on dextrose tryptone agar with brom-cresol purple ('D.T.A.' medium, supplied by Oxoid, code Nos. *G.M.* 75 and 76); and (*e*) growth and colour reaction on a tryptophan medium (using 0·1 per cent tryptophan as the sole or the additional source of nitrogen).

The results listed in Table 1 show that, on the whole, isolates (1) and (2) behave similarly. They both make good growth on a wide range of litters and give a negative reaction for phenoloxidase in the guaiac and Bavendamm tests. However, isolate (1) differs from (2) in its ability to discolour the 'D.T.A.' medium (due to a change in *p*H), also by producing a change in colour of the tryptophan medium, the change ranging from pink to cherry red, apparently caused by a metabolite derived from the tryptophan.

No interpretation of the reactions recorded in Table 1 can be put forward at this stage of the investigation. This communication is merely concerned with demonstrating the fact that the 'species' *B. scaber* does not show a uniform physiological spectrum as reflected in certain pure culture tests, which is in agreement with strain differentiation expressed in unequal effects on the growth of seedlings following inoculation of isolates (1) and (3) as reported earlier[1]. The influence of other strains of the species on the development of young trees has not been fully recorded yet.

In view of the fact that isolates (1) and (2), both from sporophores on heathland soil, react, in certain respects, similarly (Table 1) and contrast with the behaviour of the other mycelia tested, one feels tempted to suggest that differences in ecological origin might be responsible for the strain differentiation recorded. However, in order to obtain definite evidence that such a relationship exists, isolates of *B. scaber* from an additional number of localities have to be analysed and, among the ecological factors taken into account for the selection of sporophores, the tree species occurring in the neighbourhood of the fungus should be considered.

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Forest Seedlings and Mycorrhiza Development on Fly Ash

The industrial ash which is a serious agricultural problem in developed countries is an even greater danger to forest stands. This is because the deposited layer is incorporated into the mineral soil in agricultural land, whereas in forests near industrial enterprises it is constantly increasing.

Table 1

	P_2O_5	K_2O	CaO	MgO
Mgm./1,000 gm. soil in 1 per cent citric acid	373·7	93·1	2,441·6	2,008·5
Percentage dry weight	0·39	0·08	1·36	0·67

Observations[1,2] on the effects of fly ash on vegetation and the discovery of toxic elements in it led us to study its effect on the forest stands. The stands were near a coal power plant in Central Bohemia using black coal. The average amounts of the main plant nutrients in the soil is given in Table 1. The *p*H of the soil was 6·36. Spectral analysis gave the following further elements: silicon, aluminium, manganese, iron, boron, tin, copper, barium, titanium, vanadium and beryllium. The presence of elements with proved toxicity in the fly ash is evident. For this reason further attention was directed to (1) the analysis of vegetation on plots covered with ash; (2) vegetation trials with seeds of forest tree species; (3) the development of mycorrhiza on seedlings from the ash layer. On plots with a heavy layer of ash acidophil vegetation (*Vaccinium myrtillus, Deschampsia flexuosa,* acid mosses) tend to give way to species which prefer a less acidic environment (*Fragaria vesca, Brachypodium sylvaticum, Melica nutans*) and which confirm a considerably rich layer of ash. Fly ash seems to have little effect, however, on the total number of species. Similarly, laboratory tests on Norway spruce and Scots pine showed that they developed identically on ash and on the natural substrate, namely, forest humus. An outstanding characteristic of the plots with a heavy layer of ash is the vigorous regeneration in numerous species, notably broad-leaved trees. As in the previous investigations the ash did not appear to have an unfavourable effect, we therefore directed our attention to naturally sown seedlings, particularly with regard to the development of the mycorrhiza on their roots. Mycorrhiza, as one of the connecting links of the plant with the soil, by its susceptibility to various toxic substances[3], can give some indication of the environment in which the roots are living.

Investigations were carried out on several species; the results were as follow:

Mountain ash: endotrophic mycorrhiza with a tendency to parasitism.

Maple: without evident endotrophism; autotrophic nutrition.

Birch: typical ectotrophic mycorrhiza with strong fungus coat; partially automycotrophic nutrition.

Summer oak: typical ectotrophic mycorrhiza with fungus mantle and Hartig net on most roots. Automycotrophic nutrition prevails.

Larch (*L. decidua*): most seedlings with incomplete ectotrophic mycorrhiza; individually endotrophic mycorrhiza. Automycotrophic nutrition prevails on all seedlings.

Scots pine: on most roots only ectotrophic mycorrhiza; automycotrophic nutrition prevails.

Norway spruce: all roots with ectotrophic mycorrhiza; automycotrophic nutrition.

Hazel: well-established ectotrophic mycorrhiza.

All three stages of this work (analysis of ground vegetation in forest stands; laboratory vegetation trials; and analysis of lateral nutritive roots of natural regeneration) agree. The fly ash from black coal, although it contains apparently unfavourable elements, does not have harmful effects on forest tree species or on herbaceous vegetation. This conclusion cannot be generalized: the effect of fly ash on vegetation has to be investigated in each individual case. It is interesting that the mycorrhiza appear quite normal in an abnormal environment.

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Analysis of Mast Cells by means of Polarization Microscopy

It has already been established that mast cells contain heparin[1], hyaluronic acid[2], histamine and 5-hydroxytryptamine[3].

Mast cells are an inhibiting factor in the clotting of blood. They are an active factor in fibrinolysis. They decompose the structure of lipids, and bind and set free histamine and 5-hydroxytryptamine. They have a cytostatic effect. They produce the ground substance of connective tissue. They exert an antitryptic effect, and enter into the metabolism of sulphur. In spite of this little is known about the structure of the protoplasm between the granules of mast cells. The problem is how to study this protoplasm, to follow its development and to investigate the connexion between the multifarious functions of the mast cells and this protoplasm. The latter can be investigated if we change it into an anisotropic substance. We have searched for dyes which stain the granules of the mast cells well and at the same time produce anisotropy in the components of their cells, and have found that pyronin *G*, toluidine blue and neutral red (Grübler) dissolved in an acid medium (1 per thousand in *N*/10 hydrochloric acid) produce anisotropy in the intergranular protoplasm of the mast cells. The birefringence cannot be extinguished by imbibition (Fig. 1).

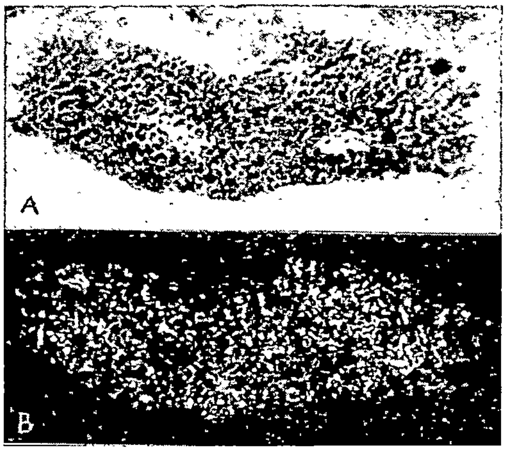

Fig. 1. Mast cell from the connective tissue of a rat. Without fixation. (*A*) Dye: 1 per mille neutral red solved in *N*/10 hydrochloric acid. (*B*) The same examined in polarized light. (× 600)

Preparations of membranes from the subcutaneous loose connective tissue of albino rats were used, and also rat mesentery embedded in paraffin. They were fixed by heat, chloroform – methyl alcohol or basic lead acetate. Some were stained without fixation, after drying at ordinary temperature. We did not find any difference as regards anisotropy between the mast cells in the fixed and non-fixed preparations,

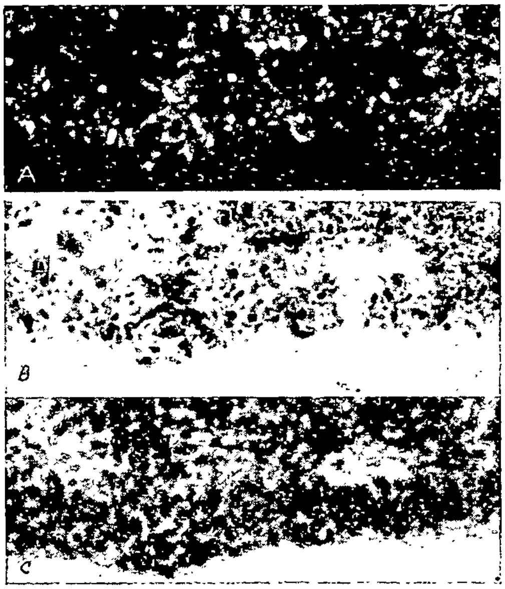

Fig. 2. Part of the cell shown in Fig. 1. (*A*) Examined in polarized light. (*B*) Contact-copy of the negative of *A*. (*C*) The same examined in normal light. (× 1,500). Note that the location of anisotropic substance in *B* is not the same as in *C*, proving that the anisotropic substance is not in the granules

or between those in the membrane preparations and those in sections.

At first it seemed that the granules of the mast cells became anisotropic; but closer analysis, however, disclosed that it was the intergranulary substance that became birefringent (Fig. 2).

The anisotropic substance is digested by ribonuclease, hyaluronidase, pepsin and trypsin. After extraction by Keilig's method[4], by which all fat-like substances are removed, birefringence is increased. This shows that the intergranulary substance is surrounded by a layer of fat-like substances which inhibit the diffusion of enzymes. But these enzymes do not digest the anisotropic substrate even after extraction by Keilig's method. Anisotropy can also be produced by using a hydrochloric acid – alcohol solution of dye. Anisotropy develops even when staining is carried out at a temperature of 80° C.

Anisotropy is prevented if saturated aqueous urea solution or 1 per cent protamine sulphate solution is used.

The dyes producing birefringence have the common property of two different poles (haptofore groups), one of which is lipophile, whereas the other is salt-producing[5]. We presume therefore that there is some complex lipoprotein material present in the intergranulary substance which possesses partly acid and partly alkyl side-chains. The side-chains of both types are oriented. The salt-producing group plays a decisive part in the development of anisotropy.

The anisotropic substance of the mast cells can be clearly followed in the connective tissue even after their disintegration.

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PATHOLOGY

Oxygen Exposure and Brain Damage

IN human premature infants, prolonged exposure to an oxygen concentration above 30–40 per cent in an incubator tends to produce retinal damage[1] (retrolental fibroplasia). A similar disease has been produced experimentally by oxygen exposure of newborn mice, rats, kittens and other animals, which are relatively immature at birth as compared with full-term human babies[2-4]. With the exception of pulmonary injury[5], no other pathological alterations have been reported after oxygen exposure of premature infants. As the brain, like the retina, develops considerably after birth, special attention was paid to the influence of oxygen exposure on the maturation of the brain. No characteristic brain injury has been found in children exposed to oxygen, though neurologic and mental defects are more common in children with retrolental fibroplasia than in other prematurely born children[6]. No brain damage in animals after similar treatment has hitherto been observed[3,4].

Definite alterations in the post-natal development of the cerebral cortex in mice after oxygen exposure are reported in this communication. Newborn mice were kept in 90–100 per cent oxygen continuously for 5–30 days after birth. Other mice were kept in oxygen for 5–15 days, after which they were transferred to air for 5–60 days before use. Still others, not exposed to oxygen, served as controls. More than 500 mice were used.

The relative amounts of cortical capillaries were measured on frozen sections after intracardial injection of indian ink. Continuous exposure to oxygen reduced the mass of vessels per standard area of section, the decrease amounting to 20 per cent at 15 and 20 days, in the visual as well as the motor cortex. Exposure to oxygen for 5, 10 or 15 days, followed by normal conditions, resulted in an intensified growth of the cortical vessels, in the visual and the motor areas. After 5 days in oxygen and then 15 days in air, a vascular hyperplasia was found, the relative amount of vessels exceeding that of the controls by some 10 per cent.

These alterations in cerebral vascularization are similar to the early stages in the pathogenesis of retrolental fibroplasia and of retinal damage induced by oxygen in experimental animals. In oxygen, the post-natal vascularization of the retina is suppressed. After transfer from oxygen to air, a pathological enhanced neo-vascularization of the retina takes place. Thus, similar changes occur in the cortex cerebri, though no qualitative pathological changes are seen.

In the eye, permanent retinal atrophia is often observed in adults after exposure to oxygen of newborn mice. Similarly, in cortex cerebri, the initial vascular hyperplasia after transfer from oxygen to air was followed by a slight reduction of the relative amount of cortical vessels. This vascular hypoplasia was, however, only present in the visual cortex, not in the motor cortex. It might be supposed that the vascular hypoplasia in the visual cortex depended on retinal damage and thus constituted a transneuronal alteration, due to disturbed visual function.

A second series of experiments was made in order to test this hypothesis. Growing mice were kept in complete darkness for 20 and 30 days, and the vascularity of the cortex was measured. A decrease in capillary amounts was observed, and this decrease was manifest in the visual cortex only, not in the olfactory area.

Besides studies on the vascularization of cortex cerebri, quantitative studies on the growth of the cortical cell nuclei and on the growth of internuclear material ('neuropil') were performed. Continuous exposure to oxygen for 10 days resulted in cortical intracellular œdema, indicated by nuclear swelling and an increase in the amount of neuropil per nucleus. Such cortical œdema may be of importance in the vascular hypoplasia, causing a capillary compression (as was suggested by Ashton[7] regarding similar reactions in the retina of animals exposed to oxygen). After the cortical swelling, prolonged exposure to oxygen caused a decrease in nuclear size and in neuropil growth. These alterations in the post-natal maturation of the brain cortex were observed in both the visual and the olfactory area. In contrast to the general effects on the cortex cerebri of exposure to oxygen, there was retardation of neuronal growth and of neuropil increase in the visual cortex only, not in the olfactory cortex, in animals kept in the dark for 20–30 days after birth.

Thus, exposure of growing mice to concentrated oxygen suppresses the post-natal maturation of cortex cerebri by both direct and indirect action (through retinal damage).

The present investigations will be published in full elsewhere.

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Role of the Thymus in Murine Leukæmia

LYMPHOCYTIC neoplasms with characteristic thymic involvement occur spontaneously with high frequency in certain strains of mice[1], and in other strains following X-irradiation[2], chemical carcinogens[3] or the inoculation at birth of cell-free extracts of leukæmic tissue from high leukæmic strain mice[4]. Total thymectomy has been shown to reduce markedly the incidence of the disease, either spontaneous[1] or induced[2,3]. No report has yet appeared as to the effect of subsequent thymectomy on the occurrence of the disease in mice inoculated at birth with leukæmia extracts. Harris[5] has, however, an interesting theory which suggests that non-cellular leukæmic-inducing extracts might be capable of replacing thymic influence. Latarjet *et al.*[6] and Furth *et al.*[7] have shown that inoculation of *Ak* leukæmic cell-free extracts into newborn *Ak* mice accelerates the development of leukæmia. The effect of thymectomy on this acceleration has been investigated and reported here.

Newborn Ak_i mice, from a colony maintained by strict sib-matings in these laboratories since 1945, were divided into three approximately equal groups, each litter being divided between the three groups. The control group had their tails cut off for identification purposes but received no further treatment apart from an intraperitoneal injection of saline. Mice in the other two groups were inoculated within 16 hr. of birth with Ak_i leukæmic cell-free filtrates prepared according to Gross's method[4]. Extracts were made from either leukæmic thymus only, or leukæmic lymph nodes only. At 3–4 weeks of age about half the inoculated mice were thymectomized, the thymus being sucked out of the thorax through an incision in the neck. The three groups were caged side by side and maintained on ordinary laboratory diet.

The results are given in Table 1. Almost all the inoculated mice which were not thymectomized succumbed to leukæmia between 3 and 6 months of age. The majority of the untreated control mice contracted the disease but not until after the seventh month. None of the mice inoculated with either leukæmic thymus or leukæmic lymph node extracts at birth and afterwards thymectomized has yet succumbed to leukæmia. In contrast to the recent findings of Furth[8] no tumour other than leukæmia has yet been seen in any mice of the present series.

The results clearly show that in *Ak* mice inoculated at birth with cell-free extracts of leukæmic tissues, thymectomy suppressed the subsequent appearance of leukæmia. There can be little doubt as to the cell-free nature of the present extracts of leukæmic tissues for no leukæmia appeared in the thymectomized and inoculated animals, whereas it can easily be shown that thymectomy does not affect the transmission of leukæmia by cell graft. The effect of thymectomy on the incidence of leukæmia in low-leukæmic strain *C3H* mice inoculated at birth with *Ak* leukæmic cell-free extracts is under investigation and will be reported later.

Table 1. INCIDENCE OF LEUKÆMIA IN Ak_i MICE INJECTED AT BIRTH WITH FILTRATES FROM Ak_i LEUKÆMIC TISSUES

Treatment	Total No. of mice	Age in days at time of diagnosis					Leukæmia incidence	
		60–90	91–150	151–180	181–210	211–300	No.	Per cent
Injected at birth	29	1	18	5	2	1	27	93
Injected at birth, thymectomized	21	0	0	0	0	0	0	0
Control	34	0	0	1	3	27	31	91

I am indebted to a scholarship from the University of Queensland, Brisbane, Australia, and to Profs. A. Haddow and P. C. Koller and Dr. R. J. C. Harris for their interest. The investigations have been supported by grants to the Chester Beatty Research Institute (Institute of Cancer Research: Royal Cancer Hospital) from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund, and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service.

Note added in proof. Since this communication was submitted for publication I have learned that similar results have been obtained in *C3Hf/Gs* mice by Drs. Levinthal, Buffett and Furth, to be published in *Proc. Soc. Exp. Biol. and Med.*

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Plaque Production with Yellow Fever and Related Arthropod-borne Viruses

WHEN a monolayer of chick fibroblasts is exposed to infection with a suitable dilution of Western Equine Encephalomyelitis virus and afterwards incubated under a layer of agar containing cell nutrients, areas of cell destruction or 'plaques' are produced; these were shown by Dulbecco[1] to result from infection by single virus particles. The plaque technique has since been applied to a number of other viruses; but the presence of cell destruction or a cytopathic effect is normally considered to be a prerequisite for the success of the technique.

Among the arthropod-borne viruses, cytopathic changes are generally strong with group *A* viruses, such as *WEE*, but are weak or absent with group *B* viruses[2]. The demonstration by Bhatt and Work[3] that West Nile virus (which falls within the group *B*) was readily adapted to produce a cytopathic effect in tube cultures of chick embryo fibroblasts suggested that this virus might be titrated in monolayers of these cells. It was observed that early passage-levels of West Nile virus (Egypt 101 strain) which failed to produce a definite cytopathic effect in tube cultures of chick fibroblasts nevertheless yielded plaques when introduced on to chick fibroblast monolayers[4]. This observation suggested that other viruses which multiply in chick fibroblasts without producing a definite cytopathic effect might, under suitable conditions, produce plaques.

Because of its importance in the group, attention was first directed to yellow fever virus. The 17*D* strain of this virus was adapted to chick embryos by Theiler and Smith[5]. Tube cultures of chick fibroblasts support the growth of virus, but show no definite cytopathic changes. When chick fibroblast monolayers are infected with 17*D* virus under the conditions of the plaque technique, a change in the staining properties of virus-infected cells can be detected on or after the fourth day, with the development of discrete plaques 2–3 mm. in diameter. These are readily counted on the fifth or sixth day as whitish areas against a background of cells stained pink with neutral red.

In early experiments some difficulty was experienced in maintaining chick cells in a healthy state under agar for the 5 or 6 days necessary for plaque production. The technique finally adopted was to grow chick fibroblasts in a medium containing 5 per cent calf serum, 5 per cent lactalbumin hydrolysate (5 gm./100 ml.) and 90 per cent Gey's solution[6] incorporating 5 per cent sodium bicarbonate (2·25 gm./100 ml.). Overnight incubation at 37° C. of $40–50 \times 10^6$ cells in 5 ml. of medium in an atmosphere of 5 per cent carbon dioxide gave dense confluent monolayers. These were exposed to dilutions of virus in 10 per cent calf serum in Gey's solution without bicarbonate for periods of 1–4 hr. at 37° C. After removal of unadsorbed virus the plates were overlaid with a medium made by mixing equal parts of 2·0 per cent agar in distilled water and the following: Gey's solution *A* (ten times concentrated) 20 per cent, Gey's solution *B* 10 per cent, *tris* (hydroxymethyl) aminomethane 0·2 *M* *p*H 7·6 10 per cent, lactalbumin hydrolysate (5 gm./100 ml.) 10 per cent, calf serum 10 per cent, neutral red (1 : 1,000) 10 per cent, distilled water 30 per cent. Under these conditions chick cells remain healthy for seven or more days when incubated in a well-humidified incubator without added carbon dioxide. A preparation of 17*D* virus which contained 8×10^6 *LD*50 per ml. when titrated intracerebrally in mice has given titres ranging from $1{\cdot}4 \times 10^6$ to $4{\cdot}5 \times 10^6$ plaque-forming units per ml. according to the conditions of the test. Details of this work and of a technique for determining yellow fever neutralizing antibody will be published elsewhere[7].

The modified plaque technique was next applied to a representative selection of other group *B* arthropod-borne viruses, including the French neurotropic strain of yellow fever virus, Uganda *S*, West Nile, Wesselsbron, Japanese *B* and Louping ill viruses. West Nile, Uganda *S*, Japanese *B* and Wesselsbron viruses produced plaques which were readily visible on the second or third day and increased to 5 mm. in diameter. Zika virus resembled 17*D* in producing smaller plaques which were not visible until the fourth or fifth day. Somewhat unexpectedly, neurotropic yellow fever virus which has been maintained by serial passage in mouse brains and has never been passaged in chick tissues gave plaques which were larger and more distinct than those produced by egg-adapted 17*D* virus. Louping ill virus produced plaques which were indefinite until the seventh day. At this time they measured 2–3 mm. in diameter and were countable though less readily than with the other viruses.

There can be little doubt that the cells which make up a plaque produced by infection by *WEE* virus are in fact dead. The plaques produced by yellow fever virus have less distinct margins and frequently include a number of cells which retain the neutral red stain towards the centre of the plaque. Whether cells which lose the property of staining with neutral red are in fact dead or are in a state which is reversible and from which they normally recover in liquid media is uncertain. However, it is clear that the conditions of the plaque technique produce a change in the staining properties of virus-infected cells which represents a form of cytopathic effect which is considerably more readily detected than that normally observed by direct microscopy.

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BACTERIOLOGY

Bacteriophage Enrichment in a Liquid Two-Phase System with Subsequent Treatment with 'Freon' 113

THE possibility of concentrating protein molecules in one of the phases in a liquid two-phase system of polymers has been investigated by Albertsson[1,2], who showed that the distribution coefficient can be related to the size of the molecules in accordance with the Brønsted[3] formula. Albertsson and Frick[4] have shown that in a dextran–methylcellulose system this relation holds for particles up to the size of phages, the upper limit at present being the size, or rather the surface area of T_2 phage. The concentration of T_2 in the bottom dextran-rich phase will be 400 times higher than in the methylcellulose-rich top phase if the two phases are allowed to separate for 48 hr. in the cold.

When phages are grown in litre quantities of substrate, it is convenient to diminish this amount to volumes more easily handled in a usual high-speed centrifuge. Essential drawbacks of the centrifugation technique (see, for example, ref. 5) are that a portion of the phages in a pellet will be broken and destroyed by the centrifugal force and that the resuspended particles will be somewhat aggregated. A more homogeneous high-titre suspension can probably be obtained directly by the two-phase liquid enrichment technique. The necessary purification of the suspension for the removal of bacterial debris can be obtained by treatment with a commercially available fluorocarbon, 'Freon' 113.

The procedure is as follows. *Escherichia coli*, strain *B*, is grown in 2,000 ml. of a well-defined medium, Friedlein buffer[6]. The growth takes place in a container of stainless steel fitted with an outlet quite near the bottom and with a device for good aeration. The container is thermostatted at 37° C.

When the titre of *E. coli* is about 10^8, judged from absorption at 600 mμ in the Beckman *B* spectrophotometer, enough phages are added to bring the phage titre well up to 10^6. 5–6 hr. later the medium becomes fairly clear, and the phage titre is $2–5 \times 10^{10}$. The weight of the substrate is now adjusted back to 2,000 gm. by adding distilled water, compensating for evaporation losses. The two polymers methylcellulose ('Methocel' U.S.P. 4,000 c.p.s. from Dow Chemical Co., U.S.A.) and dextran (intrinsic viscosity 0·68 from AB Pharmacia, Sweden) are added. 601 gm. of 2 per cent methylcellulose and 131 gm. of 10 per cent dextran are weighed into the container and the contents mixed thoroughly by whirling. The container is put in the cold room (+6° C.) in an inclined position, the above-mentioned outlet being at the lowest point. After 36–48 hr., the dextran-rich bottom phase which has now formed is drawn off through a capillary stopcock. The top phase is quite clear in appearance, whereas the bottom phase is turbid. As the viscosity of the top phase is much higher, the passage of the boundary through the outlet will also show a decrease in the dropping speed from the stopcock to about one-half.

The bottom phase will have a volume of about 200 ml. containing 96–97 per cent of all phages and having a titre of $2–5 \times 10^{11}$, that is, about ten-fold increase in titre. The loss is due to the 3–4 per cent remaining in the upper phase. Besides this loss, there is a loss of about 10 per cent of the total compared with the total amount of phage at the time of the addition of polymers 48 hr. earlier.

The phage suspension is treated with one-third its volume of 'Freon' 113 ($CCl_2F–CClF_2$) in a Waring blendor cooled with ice[7]. The blendor is operated at high speed for 4 × 15 sec. with intervening pauses of 30 sec. After this treatment, the suspension is centrifuged at 800*g* for 10 min. The layer of denatured protein and 'Freon' will form a semi-solid pellet, and the supernatant can easily be decanted. The procedure is then repeated until after 6–7 treatments only a thin layer is formed between the 'Freon' and the dextran–water phases. In the 4–5 last treatments, the Waring blendor is operated for 4 × 25 sec.

The phages appear to withstand the 'Freon' treatment well. For six treatments the following titres were found: 1·8, 2·0, 1·6, 1·7, 1·9, $2·0 \times 10^{11}$. An increase after the first treatment, especially for very opaque suspensions up to 30 per cent, is often noted. It is, however, also necessary to be careful to avoid coprecipitation of phages with the denatured protein and the methylcellulose. The treatment with 'Freon' precipitates the methylcellulose, but not the dextran. (The loss in volume can be kept to 5 per cent.)

The dextran seems to have a strong protective effect, as 'Freon' treatment of phages suspended in only Friedlein buffer will result in a drop in titre of 10^3 each time. Phage suspended in full media (Difco nutrient broth) will be fully protected, but the medium will change since the treatment with 'Freon' gives a heavy precipitate in unused fresh media.

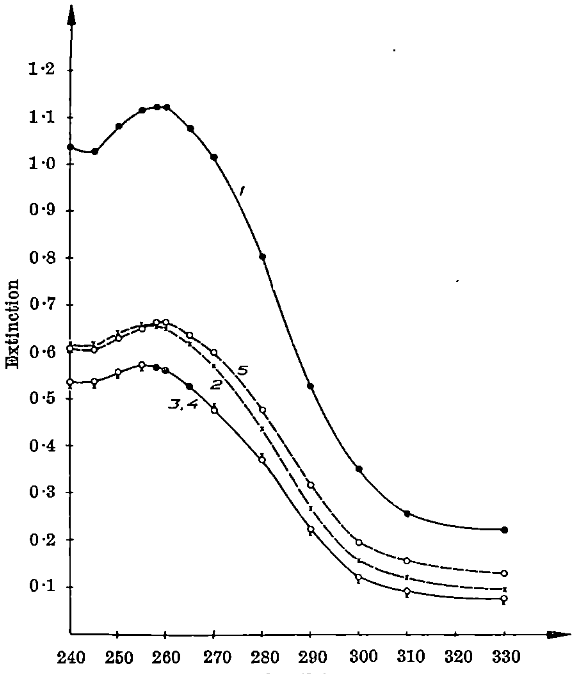

Fig. 1. Absorption of a T_2 preparation treated with 'Freon' 113. Curve 1, untreated phage suspension in dextran-rich bottom phase (titre, $3·4 \times 10^{11}$); curve 2, same suspension after one treatment with 'Freon' (titre, 2×10^{11}); curves 3 and 4, same suspension after four and six treatments with 'Freon' (titre, 2×10^{11}; curve 5, the values of curve 1 recalculated to the same, in this case lower, titre of curve 2. The result shows that the loss of titre corresponds to a loss in material through precipitation (probably co-precipitation). All absorption measurements on suspension, twenty times diluted with Friedlein buffer, against the same buffer

The effect of the treatment with 'Freon' on the ultra-violet spectrum of the suspension is shown in Fig. 1 and Table 1. For further purification, smaller fragments of protein can be removed by dialysis overnight against buffer. (Longer dialysis will cause losses.) If, for special purposes, it is necessary to free a suspension from all free nucleotides, this can be done by shaking with a small amount of calcium hydroxylapatite[9,10]. This operation will, however, cause some slight loss in titre. The quotients of the absorption value at 260 mμ and 280 mμ reported in Table 1 indicate a decrease in protein after treatment with 'Freon' and dialysis, and a decrease in nucleotides due to adsorption on hydroxylapatite.

To compensate for possible losses in the last operation or after sterile filtration, or to double the titre anywhere in the described procedure, 1 part of 2 per cent methylcellulose is added to 1 part of the

Table 1. QUOTIENTS OF ULTRA-VIOLET ABSORPTION AT 260 AND 280 Mμ FOR A T_2 PHAGE SUSPENSION AFTER DIFFERENT TREATMENTS

	$\frac{OD\ 260}{OD\ 280}$	$\frac{OD\ 260}{OD\ 280}$ (corrected values)
Untreated suspension	1·39	1·35
1 treatment with 'Freon'	1·50	1·61
6 treatments with 'Freon'	1·53	1·63
+ dialysis	1·62	1·73
+ treatment with calcium hydroxylapatite	1·60	1·68

The values in column 2 are given after correction for background absorption calculated from ultra-violet absorption values between 330 and 370 mμ (ref. 8).

bottom phase. After shaking, the two solutions are allowed to separate in the cold for 48 hr. The new dextran-rich bottom phase will be of about half the original volume, and accordingly will have a double titre. (All phage titres are determined with the agar layer technique[6].)

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Chloramphenicol and the Survival of Airborne Bacteria

In recent years the large increase of staphylococcal infections in hospitals has resulted in much research into the sanitation and disinfection of hospital wards; but little work appears to have been conducted on the airborne survival of the causative agents. In the course of studies on the viability of airborne bacteria, certain observations were made which may, in part, explain the spread of these cells, especially the antibiotic-resistant strains.

Cells from each of a 24-hr. broth culture of *Staphylococcus albus*, *Serratia marcescens* and *Escherichia coli* were harvested by centrifugation, washed once and resuspended in distilled water. These suspensions were then aerosolized, by means of a Collison spray[1] into a stainless-steel rotating drum[2] of 1,100-litre capacity. Samples were collected in liquid impingers immediately after aerosolization and at subsequent hourly intervals up to 5 hr. The initial concentration in the drum was approximately 1×10^6 cells/l. of air. Loss due to physical fall-out was calculated using a modification of the radioactive tracer technique described by Harper *et al.*[3].

Viable decay-rates were calculated for the 5-hr. air suspension from the equation:

$$K = 1/t \times \ln N_0/N_t$$

where t is time of air suspension in minutes, N_0 is initial concentration of viable cells/l. of air, and N_t is concentration of cells/l. of air at time t.

The decay-rates of the antibiotic-sensitive cells were compared with (*a*) those of a resistant strain obtained from the parent strain by growth on chloramphenicol gradient plates and (*b*) with those of sensitive cells aerosolized from a suspension in a solution of 0·25 per cent chloramphenicol. In the course of study, cells were aerosolized from solutions of other bacteriostatic substances and vitamins and the results of two of these with chloramphenicol are shown in Table 1.

Table 1. Death-Rates of Some Bacteria Aerosolized from Various Media

Organism		Suspending medium			
		Water	Chloramphenicol (0·25 per cent)*	*o*-Amino phenol (0·5 per cent)*	Inositol (6·0 per cent)*
Staphylococcus albus	*S*	0·007	0·002	0·001	0·001
	R	0·002	0·003	0·002	0·002
Serratia marcescens	*S*	0·034	0·010	0·007	0·001
	R	0·012	0·008	0·008	0·002
Escherichia coli	*S*	0·029	0·013	0·006	0·001
	R	0·011	0·010	0·007	0·002

Relative humidity, 30–32 per cent; temperature, 25° C. *S*, sensitive to chloramphenicol; *R*, resistant to chloramphenicol.

* The concentrations of added compounds shown are those found to give optimal aerosol survival.

It can be seen that the *Staphylococci* are far more resistant to aerosol death than the two other genera, and it would appear that resistance to chloramphenicol affords considerable stability to the cells. More surprising, however, was the suggestion that a like stability could be afforded the cells by suspension in the antibiotic prior to aerosolization, and that aminophenolic compounds were also protective. Far greater stability was afforded the cells by inositol, but considerably higher concentrations were required. In the presence of chloramphenicol, however, the quantity of inositol could be reduced by half without decreasing the stability of the cells. Thus there appeared a synergistic action between the drug and the vitamin. The observed increase in survival of cells by these compounds was found to depend on the relative humidity of the air, chloramphenicol affording greater protection to the cells at high relative humidity while inositol was more effective at low relative humidity-levels.

In more recent experiments other bacteriostatic drugs, such as some of the sulpha drugs, and *cyclo*hexane substituted with hydroxyl- or amino-groups have been found to enhance bacterial aerosol survival, and the position of the substituents on the ring appears important. As a result of this work a hypothesis has been formulated that airborne cells die as a direct result of the loss of bonded water from their protein with the subsequent collapse of protein structure. It is felt (*a*) that the compounds affording increased stability to the cells are able to preserve protein structure by taking the place of water molecules during desiccation, and (*b*) that the type of bonding between protein-water and protein-compound is weak, reversible and dependent on the relative concentrations of compound and water. It is thus possible that chloramphenicol enhances bacterial aerosol survival by the same mechanism as it inhibits protein synthesis, that is, it takes the place of water molecules or blocks the water-bonding sites of the protein but does not destroy its structure, thus enzymatic action and synthesis is prevented. When, however, the drug is diluted by body fluids or water the reverse reaction occurs, water molecules displace chloramphenicol molecules and cellular metabolism is resumed.

The fact that bacteriostasis, by several organic compounds, normally used in chemotherapy and disinfection, may preserve airborne cells might, in part, explain why some measures of sanitation have failed in hospitals.

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FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

Monday, April 13

Institution of Electrical Engineers, Education Discussion Circle (at Savoy Place, London, W.C.2), at 6 p.m. Discussion on "The Function and Content of an Electric Theory Course" opened by Mr. F. E. Rogers.

Royal Geographical Society (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Lieutenant N. C. Flemming: "Last Summer's Cambridge Expedition to Explore the Submerged Ruins of an Ancient Port and City Off the Libyan Coast".

Tuesday, April 14

Institution of British Agricultural Engineers (at 6 Buckingham Gate, London, S.W.1), at 2.15 p.m.—Mr. P. H. Bailey: "The Measurement of Crop Drier Performance".

Zoological Society of London (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

Institution of Mechanical Engineers, Automobile Division (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. D. L. Pratt: "The Performance of Vehicles Under Trans-Antarctic Conditions".

Institution of Electrical Engineers, London Graduate and Student Section (joint meeting with the Graduate and Student Sections of the Institutions of Civil and Mechanical Engineers, at Savoy Place, London, W.C.2), at 6.30 p.m.—The Rt. Hon. the Viscount Chandos, P.C., D.S.O., M.C.: "Finance and the Engineer".

Society of Chemical Industry, Corrosion Group (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. W. Feitknecht (University of Berne): "Studies of the Influence of Chemical Factors on the Corrosion of Metals" (Spring Lecture).

Institute of Metals (in the Lecture Theatre of the Royal Institution, Albemarle Street, London, W.1), at 7 p.m. Prof. F. Hoyle, F.R.S.: "The Scientific Uses of Space Exploration".

Tuesday, April 14—Wednesday, April 15

Laboratory Animals Centre (at the Royal Veterinary College, Royal College Street, London, N.W.1)—Twelfth L.A.C. Congress.

Wednesday, April 15

Royal Society of Arts (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Prof. George C. Varley: "The Biological Control of Agricultural Pests" (Fernhurst Lecture).

Physical Society, Colour Group (at the Victoria and Albert Museum, South Kensington, London, S.W.7), at 3.15 p.m.—Annual General Meeting. Mr. J. W. Perry: "Psychophysical Measurement" (Chairman's Address).

Royal Statistical Society (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Mr. P. A. Stone: "The Economics of Housing and Urban Development".

University College (in the Chemistry Theatre, Gower Street, London, W.C.1), at 6 p.m.—Colonel H. T. Jessop: "Photoelasticity at University College London: Jubilee Commemoration of the Work of E. G. Coker and L. N. G. Filon, 1909–1937"; with an Exhibition of Work in Photoelasticity at University College London, in the Department of Physics (also open April 16 and 17).*

Pharmaceutical Society of Great Britain (at 17 Bloomsbury Square, London, W.C.1), at 7.30 p.m.—Dr. J. B. Stenlake: "Progress in the Chemistry of Natural Products".

Thursday, April 16

Laboratory Animals Centre (at the Royal Veterinary College, Royal College Street, London, N.W.1), at 9.30 a.m.—Symposium on "Quality in Laboratory Animals".

Royal Society (at Burlington House, Piccadilly London, W.1), at 4.30 p.m.—Prof. E. L. Hirst, F.R.S.: "Molecular Structure in the Polysaccharide Group" (Bakerian Lecture).

Institution of Mining and Metallurgy (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. F. Mendelsohn: "Structure of the Road Antelope Deposit".

Linnean Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. Kenneth Sporne: "Correlation of Biological Characters"; Prof. H. Grüneberg, F.R.S.: "On Correlation of Characters in the Mouse".

London Mathematical Society (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. D. A. Edwards: "Commutative Algebras of Operators".

Institution of Electrical Engineers, Utilization Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Dr. D. O. Bishop and Dr. G. S. Brosan: "An Electromagnetic, Variable-Ratio, Torque Convertor".

Royal Anthropological Institute (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Dr. G. Ainsworth Harrison: "Environmental Determination of Mammalian Morphology".

Society of Chemical Industry, Road and Building Materials Group (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Annual General Meeting, followed by Mr. R. I. Hughes: "Adhesion in Bitumen Macadam".

Society of Instrument Technology, Control Section (at Manson House, Portland Place, London, W.1), at 6 p.m.—Annual General Meeting, followed by Mr. A. P. Roberts: "Self-Optimising Control System for a Certain Class of Randomly Varying Inputs".

British Computer Society (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Prof. L. Hogben, F.R.S.: "The Mechanical Translation of Languages".

British Institution of Radio Engineers, Radio Group (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Inaugural Meeting.

Society for Analytical Chemistry, Biological Methods Group (at "The Feathers", Tudor Street, London, E.C.4), at 6.30 p.m.—Discussion on "Problems of Recording and Communicating Technical Information in a Commercial Research Organization", opened by Miss Pamela D. Waterhouse.

Society of Chemical Industry, Fine Chemicals Group (at the Royal Institution, Albemarle Street, London, W.1), at 6.30 p.m.—Prof. A. Stoll: "The Cardiac Digitalis Glycosides".

British Institute of Radiology, incorporated with the Rontgen Society (at 32 Welbeck Street, London, W.1), at 8 p.m.—Prof. G. Stead: "1895 and All That" (Silvanus Thompson Memorial Lecture).

Thursday, April 16—Thursday, April 30

Engineering, Marine, Welding and Nuclear Energy Exhibition (at Olympia, London).*

Friday, April 17

Institute of Physics (at the Royal Society of Tropical Medicine and Hygiene, 26 Portland Place, London, W.1), at 9.45 a.m.—Symposium on "Current Developments in the Production of High Vacua".

Plastics Institute (joint meeting with the London Section of the Institution of the Rubber Industry, in the William Beveridge Hall of the London University, Malet Street, London, W.C.1), at 10 a.m.—Conference on "Adhesion".

Association of Applied Biologists (in the Metallurgy Lecture Theatre, Royal School of Mines, Imperial College, Prince Consort Road, London, S.W.7), at 2.15 p.m.—Annual General Meeting, followed by Dr. I. Thomas: "Control and Conservation" (Presidential Address).

Institution of Mechanical Engineers (at 1 Birdcage Walk, Westminster, London, S.W.1), at 4 p.m.—Symposium on "Biomechanics".

Institute of Navigation (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Colonel C. Powell: "The Dectra Trials".

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Senior Lecturer in Organic Chemistry; a Lecturer in Chemical Technology; Lecturers (2) in Mathematics; an Assistant (Grade B) in Mathematics; Lecturers (2) in Physics; and an Assistant (Grade B) in Physics—The Registrar, College of Technology, Ashley Down, Bristol 7 (April 16).

Assistant, Grade A (with a degree or equivalent qualifications), in the Department of Pure and Applied Science, Northampton College of Technology, to teach chemistry and physics—The Chief Education Officer, Borough Education Office, "Springfield", Cliftonville, Northampton (April 18).

Lecturer, Grade II (a) (with a good honours degree in physics and teaching and/or industrial experience) in Physics at Dundee Technical College—The Clerk and Treasurer, Institute of Art and Technology, 40 Bell Street, Dundee (April 18).

Lecturer in the Department of Metallurgy, to teach and carry out research in Physical Metallurgy—The Registrar, The University, Liverpool (April 18).

Assay Master—Sir Douglas S. Branson, Law Clerk to the Guardians, Assay Office, 6 Paradise Square, Sheffield 1 (April 20).

Lecturer or Assistant Lecturer (with a good honours degree in chemistry and special qualifications in physical chemistry) in Chemistry—The Registrar, King's College (University of London), Strand, London, W.C.2 (April 20).

Assistant Lecturers (2) in Physics—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (April 22).

Lecturer (with a good honours degree and some experience in research and in industry) in Chemical Engineering—The Registrar, King's College (University of London), Strand, London, W.C.2 (April 22).

Assistant Lecturer in Pure or Applied Mathematics—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8 (April 25).

Chair of Sociology—The Registrar, The University, Leicester (April 25).

Lecturer or Assistant Lecturer in Physics—The Registrar, Manchester College of Science and Technology, Manchester 1 (April 25).

Senior Lecturer in Political and Social Geography—The Registrar, The University, Leicester (April 25).

Assistant Lecturer (with a degree in botany with some zoology) in Biology—The Registrar, University College of North Staffordshire, Keele, Staffs (April 30).

Assistant Lecturers in Pure Mathematics, Electronic Engineering, Chemistry (Inorganic and Physical), Agriculture (Animal Genetics), Marine Biology and Psychology—The Secretary and Registrar, University College of North Wales, Bangor (April 30).

Lecturer (honours graduate in science, with qualifications in two of the following: botany, chemistry or geography) in Education—The Secretary and Registrar, University College of North Wales, Bangor (April 30).

Senior Lecturer in the Department of Physiology, University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (South Africa, April 30).

Lecturer or Assistant Lecturer in Applied Mathematics—The Registrar, The University, Hull (May 1).

Lecturer (graduate, preferably with honours or higher degree in chemistry) in Chemistry in the Department of Science and Metallurgy—The Principal, North Lindsey Technical College, Kingsway, Scunthorpe, Lincs (May 4).

Lecturer in Nuclear Engineering—The Registrar, Queen Mary College, Mile End Road, London, E.1 (May 6).

Lecturer or Assistant Lecturer in Inorganic and Structural Chemistry—The Registrar, The University, Leeds 2 (May 6).

Chair of Applied Mathematics—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (May 8).

Senior Lecturer in Medicine at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, May 9).

Lecturer (with British university qualifications, or equivalent, and preferably experience in teaching geography in a university department of geography and geology) in Geography at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong, May 15).

Senior Lecturer (with an appropriate higher qualification and experience in teaching and in research methods) in Medicine at the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong, May 15).

Chair of Physiology in the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong, May 30).

Computing Assistant (female, with at least A-level mathematics or equivalent, with hand computing experience), for work in connexion with rocket and satellite studies of the upper atmosphere—The Secretary, University College, Gower Street, London, W.C.1.

Experimental Physicists (with at least a good second-class honours degree, and preferably postgraduate experience in some aspect of nuclear physics), for (*a*) to collaborate with physicists designing a 7 GeV. Proton Synchrotron, to take responsibility for aspects of selection, analysis and transport of high energy beams and eventually to participate in high energy nuclear research; and (*b*) to work with nuclear physicists using a 50-MeV. Proton Linear Accelerator shortly to be commissioned and to collaborate with university physicists using this machine—The Secretary, National Institute for Research in Nuclear Science, Rutherford High Energy Laboratory, Harwell, Didcot, Berkshire, quoting N.1/1/1388/34.

Fisheries Research Officer (with a good honours degree in natural science (zoology) and training or experience in fish ecology) in Nyasaland, for research into the biology and ecology of Lake Nyasa fish—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.152/4/01.

Science Master to teach Physics to A and Chemistry to O level—The Headmaster, Cheltenham College.

Scientific Assistant (Abstractor) (with a degree in agriculture or natural science, and a knowledge of languages)—The Director, Commonwealth Bureau of Pastures and Field Crops, Hurley, Berkshire.

Senior Lecturers and Lecturers in Mathematics and Statistics—The Registrar, Bradford Institute of Technology, Bradford 7.

Senior Plant Pathologist (with a good honours degree in botany, considerable experience in plant pathology, and administrative ability) in Northern Nigeria, for general plant pathology investigations—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/408/039.

Senior Technician (with experience in experimental physiology) in the Physiology Department—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1.

Zoologist (with at least an honours degree in zoology, biology or entomology of a recognized university, plus at least two years approved postgraduate experience) at the Institute of Medical Research, Kuala Lumpur, Federation of Malaya, for duties which involve research on the ecology of arthropod vectors and on animals as disease reservoirs, with special reference to arthropod-borne virus diseases—The Recruitment and Personnel Division, Government of the Federation of Malaya, Malaya House, 57 Trafalgar Square, London, W.C.2.

REPORTS and other PUBLICATIONS

(*not included in the monthly Books Supplement*)

Great Britain and Ireland

Building Research Station Digest No. 118 (January, 1959): Reducing Laboratory Vibrations. Spray Taps. Pp. 4. (London: H.M. Stationery Office, 1959.) 4*d*. [112

Economic Proceedings of the Royal Dublin Society. Vol. 4, No. 6 (October 8, 1958): Population Studies on Cereal Root Eelworm *Heterodera major* (O. Schmidt, 1930). By J. J. Duggan. Pp. 103–118+plate 17. (Dublin: Royal Dublin Society, 1958.) 4*s*. [112

Bardsey Bird and Field Observatory. Report for 1957. Pp. 44. Eglwysfach, Machynlleth, Mont.: W. M. Condry, Hon. Secretary, (1959.) [112

Proceedings of the Royal Irish Academy. Vol. 59, Section A, No. 3: Expansions for the Logarithmic-Integral and Cosine-Integral Functions. By A. S. Meligy. Pp. 25–28. 6*d*. Vol. 59, Section A, No. 4: Structure Theory. By D. J. Newman. Pp. 29–47. 3*s*. Vol. 59, Section B, No. 12: The Littoral Harpacticids of the Dalkey (Co. Dublin) Area with Descriptions of Six New Species. By Katharine M. Roe. Pp. 221–255. 5*s*. Vol. 59, Section B, No. 13: Studies of Flowering-Plant Growth and Organo-Genesis—III: Leaf Shape Changes Associated with Flowering and Sex Differentiation in *Cannabis sativa*. By J. Heslop-Harrison and Y. Heslop-Harrison. Pp. 257–283. 4*s*. Vol. 59, Section B, No. 14: The Carboniferous Knoll-Reefs of East-Central Ireland. By W. E. Nevill. Pp. 285–303+plate 5. 2*s*. 6*d*. Vol. 59, Section B, No. 15: The Chemical Composition of some Irish Peats. By T. Walsh and T. A. Barry. Pp. 305–328. 3*s*. 6*d*. Vol. 59, Section B, No. 16: Pollen Analytical Investigations of the Mire at Fallahogy TD., Co. Derry. By A. G. Smith. Pp. 329–343+plates 6–9. 4*s*. Vol. 59, Section B, No. 17: Antitubercular Substances—XV: Some Derivatives of Tetrahydrofuran. By Vincent C. Barry and Joan E. McCormick. Pp. 345–351. 1*s*. (Dublin: Hodges, Figgis and Co., Ltd., 1958.) [112

Other Countries

Chicago Natural History Museum. Fieldiana: Zoology. Vol. 39, No. 24 (December 18, 1958): Three New Skinks Related to *Sphenomorphus variegatus* (Peters). By Robert F. Inger. Pp. 257–268. (Chicago: Chicago Natural History Museum, 1958.) 30 cents. [102

United States Department of Agriculture. Agriculture Handbook No. 149: Growing Lettuce in Greenhouses. By Ross C. Thompson, S. P. Doolittle and T. J. Henneberry. Pp. 22. 15 cents. Production Research Report No. 23: Pitting for Range Improvement in the Great Plains and the Southwest Desert Regions. By Oscar K. Barnes, Darwin Anderson and Arnold Heerwagen. Pp. 17. 10 cents. (Washington, D.C.: Government Printing Office, 1958.) [102

Florida State Museum. Report of the Director for 1957–58. Pp. 20. (Gainesville, Fla.: Florida State Museum, The University, 1959.) [102.

The United States National Museum: Smithsonian Institution. Annual Report for the year ended June 30, 1958. Pp. iv+150. (Washington, D.C.: Government Printing Office, 1958.) [102

International Atomic Energy Agency. Safety Series No. 1: Safe Handling of Radio-isotopes. Pp. 100. (Wien: International Atomic Energy Agency, Kärtner Ring 11, 1958.) 6*s*.; 1 dollar; 350 French francs. [102

International Conciliation, No. 521 (January, 1959): The International Geophysical Year. By Walter Sullivan. Pp. ii+259–336. (New York: Carnegie Endowment for International Peace, 1959. Copies obtainable from Columbia University Press, 2960 Broadway.) 25 cents. [102

Kungl. Skogshögskolans Skrifter. (Bulletin of the Royal School of Forestry, Stockholm.) Nr. 31: Sønderdelingsprocesser i sur Humus. Av E. Oksbjerg. (Formation of Carbondioxide in Raw Humus Samples.) Pp. 30. (Stockholm: Kungl. Skogshögskolan, 1958.) [102

Durban Museum and Art Gallery. Annual Report for the Municipal Year 1957–1958. Pp. 19. Durban Museum Novitates. Vol. 5, Part II, (15th December, 1958): A New Race of Tomb Bat *Taphozous perforatus*, E. Geoffroy, 1818, from Northern Nigeria, with some Observations on Its Breeding Biology. By David L. Harrison. Pp. 143–149. 2*s*. 6*d*. (Durban: Durban Museum and Art Gallery, 1958.) [102

Illinois Natural History Survey Bulletin, Vol. 27, Article 2 (December, 1958): A Century of Biological Research. By Harlow B. Mills, George C. Decker, Herbert H. Rose, J. Cedric Carter, Bessie B. East, George W. Bennett, Thomas G. Scott, James S. Ayars and Ruth R. Warrick. Pp. vi+85–234. (Urbana, Ill.: Illinois Natural History Survey, Natural Resources Bldg., 1958.) [102

Report of the South African Museum for the year ended 31st March, 1958. Pp. 19. (Cape Town: South African Museum, 1958.) [102

Smithsonian Miscellaneous Collections. Vol. 138, No. 4: Birds of the Pleistocene in North America. By Alexander Wetmore. Pp. ii+24. (Washington, D.C.: Smithsonian Institution, 1959.) [102

Proceedings of the United States National Museum. Vol. 108, No. 3403: Rhizocephala of the Family Peltogastridae Parasitic on West Indian Species of Galatheidae. By Edward G. Reinhard. Pp. 295–307+plate 1. Vol. 108, No. 3405: Three New Serranid Fishes, Genus *Pikea*, from the Western Atlantic. By Leonard P. Schultz. Pp. 321–329. Vol. 108, No. 3406: The Status of the Lizard *Cnemidophorus perplexus* Baird and Girard (Teiidae). By T. Paul Maslin, Richard G. Beudleman and Charles H. Lowe, Jr. Pp. 331–345. (Washington, D.C.: Government Printing Office, 1958.) [102

Institut Royal des Sciences Naturelles de Belgique. Mémoires. No. 139: Étude Comparative de la Croissance de la Mandibule chez l'Homme et les Singes Anthropoides. Position des Mandibules d'Hommes Fossiles par Rapport a ces Formes Actuelles. Par Nicole Petit-Maire-Heintz. Pp. 64. No. 140: Écologie d'Une Prairie Marécageuse (Chênée—Sauheid, Province de Liège.) Par Serge Jacquemart et Eugène Leloup. Pp. 69+3 planches. No. 141: Contribution a l'Étude du Dinantien de la Belgique. Par F. Demanet. Pp. 152. No. 142: Les Foraminifères Mio-Pliocènes et Quaternaires du Kruisschans. Par Johannes H. van Voorthuysen. Supplément sur Quelques Rotalidés par Jan. Hofker. Pp. 63 (10 planches). No. 143: Foraminifera of the Oligocene of Belgium. By D. A. J. Batjes. Pp. 188+13 plates. Deuxième Série. Fasc. 56: Revision du Genre Gasteruption (Hymenoptera, Evanoidea, Gasteruptionidae). Espèces Australiennes. Par Prof. Jean Pasteels. Pp. 125. Fasc. 57: Revision der Gattung Microstigma Rambur (Ordnung Odonata, Zygoptera). Von Dr. Erich Schmidt. Pp. 44+8 plates. (Bruxelles: Institut Royal des Sciences Naturelles de Belgique, 1958.) [102

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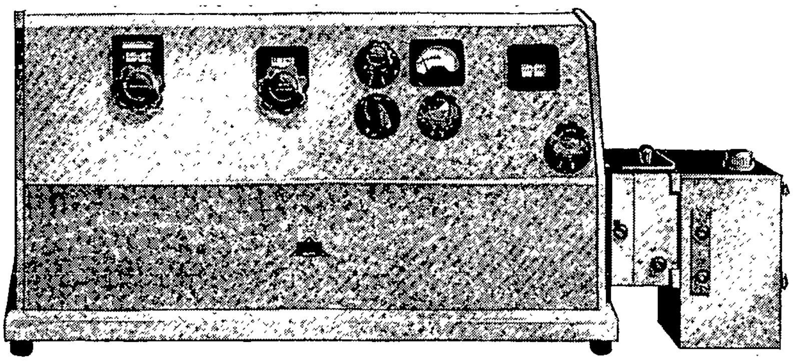

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THE NEED FOR A BALANCED EDUCATION

In the fourth of his Reith Lectures on November 30, Prof. A. C. B. Lovell remarked: "The technical devices which form the basis of the present economic and cultural strength of the Great Powers can be traced back within a few generations to fundamental scientific investigations which were carried out in the abstract, supported without thought of direct practical benefit". At least partial realization of this truth is one of the main factors which have been responsible for the steady expansion of the Parliamentary vote in Britain for the universities and for the Government's plans for the expansion of technological and technical education. Nevertheless, the national expenditure on education lags far behind the expenditure on education in the United States and in the U.S.S.R., as well as in other countries. Russian expenditure on education in 1959 is estimated at about £8,420 million, compared with £5,340 million in 1958, with £2,480 million for science and a military budget in 1959 of £8,740 million.

Dr. B. V. Bowden has recently given some comparative figures for the United Kingdom and for the United States, where some 5,000 million dollars are estimated as required in the next ten years to provide facilities for the expected increased undergraduate population; some 300 million dollars of this total is required for science laboratories. The University Grants Committee in Britain deals with twenty-one universities, one university college and two colleges of technology; in addition, there are 153 teachers' training colleges, eight colleges of advanced technology, some thirty-six advanced colleges of art and commerce, half a dozen colleges giving specialized courses, and about a hundred technical colleges giving full-time tuition to senior students. In the United States there are some 1,800 institutions of advanced study, ranging from universities with more than 40,000 undergraduates to colleges with only fifty. While only 9 per cent of the school-children in Britain enter the sixth form of grammar and secondary schools, and between 4 and 5 per cent go to universities or colleges, in the United States nearly all children remain at high school until the age of seventeen or eighteen, and last year 34 per cent of the 18–21 age group enrolled in college.

The probability that an American child will go to college is thus about four times as great as the probability that an English child will enter a sixth form, and the 95,000 students in British universities and 15,000 in training colleges compares with a present 2·7 million students in the United States and an increase to nearly 7 million by 1970, when the university population in Britain is expected to reach 142,000. When all allowance is made for the great variation in standards in American universities, for the high proportion—almost 50 per cent—of students who are unable to complete the course, and for the probability that much of the first year's work in an American university is done in the schools in Britain, the disparity is disturbing. Nor is it less so in regard to postgraduate students; the 10,000 students reading for postgraduate degrees or doctorates based on research in Britain compare with about 250,000 in the United States; and although the percentage of students who are postgraduates is about the same in both countries, there were 2,600 postgraduate students at the Massachusetts Institute of Technology alone, compared with 1,577 postgraduate students of technology in the whole of the United Kingdom.

It would be absurd for Britain to attempt to expand university and technological education on such a scale. The comparison rather emphasizes the importance of seeing that institutions in Britain at all levels are adapted to the tasks they are called upon to undertake, that the utmost care is taken to discover talent, to eliminate waste at the various levels and to ensure that the most effective use is made of trained man-power when it enters industry or other employment. Prof. Lovell in the lecture already mentioned said that unless the West overcomes its present parsimonious attitude to science and technology, the relative quality of our civilization will decline and our influence will pass to other people; and, although he was thinking more particularly of research, that comment applies no less forcibly to education. There, least of all, have we provided the facilities necessary for our existing scientific man-power.

Leaving for the moment the magnitude of expenditure in Britain on education, there is the question of priorities. Unless these are properly determined, and periodically adjusted to changing circumstances and needs, we are unlikely to obtain full value for our expenditure whatever its magnitude. If priorities are rightly chosen and care is taken to see that trained man-power is wisely and efficiently used, Britain's needs will be met with a much smaller total expenditure and one well within her comparatively limited resources, provided the appropriate measures are consistently supported and are not made the playthings of party politics.

That is largely a matter of educating public opinion, and at this point education is linked with the work of such bodies as the British Association. Addressing the annual meeting of the Indian Science Congress in New Delhi on January 22 on the work of the British Association, the Duke of Edinburgh expressed the opinion that one of the three objectives of the Association, namely, to provide for non-specialists an annual stocktaking in intelligible language which would review the progress of science and help to make clear its significance and possible consequences, is more important than ever. Every human invention or discovery can be used, he said, for good or for evil, and in the end it is the people as a whole who will decide which it is to be. It is therefore essential that the possible consequences of scientific research should be put before the forum of ordinary people. Only in this way can the combined opinion of reasonable, upright and humane men and women throughout the world exert the necessary pressure to ensure that science is used to set free and not to enslave mankind.

That is notably true in respect of education as a whole, and the Duke of Edinburgh's remark earlier in his address, that the Association had become a very useful platform for scientists to express their opinion on Government scientific policy, also applies to educational matters. Besides this important function, the British Association has indeed formed, as part of a wider programme to develop the educational programme for young people, a study group to examine the educational system for scientists.

The determination of priorities, however, is outstandingly a matter of co-operation. In his fifth Fawley Lecture on November 6, 1958, Sir Harry Pilkington, speaking of "Facing the Future in Industry", stressed the need for industry to increase the time given to internal training as well as to external education, to learning and earning at the same time, and referred particularly to the growing demand for informed judgment and consequently higher standards of management and leadership. If full use is to be made of the opportunities which science now presents, time, effort and money must be directed to the right objectives, and he believes that disciplining research effort is essential; in many industries the glamour attached to research impedes co-ordination between research, technical development and production, and may lead to loss of leadership.

Whether industry is able to work out, as Sir Harry suggests, a constructive code and philosophy of co-operation and then take on a much more positive attitude to combination and co-operation on technical and commercial subjects, and whether it can also hold its own against the growing industrial power of totalitarian countries, depends largely on the talent it is able to attract. That of itself suggests that a first priority in education should be, if not the actual search for talent, at least positive measures to ensure that the chances of talent failing to be encouraged and developed from any cause are kept to a minimum. In a recent article in *European Productivity* (No. 29; June 1958) on "Western Europe's Buried Talents", Dr. R. Schairer suggested the formation of a study group of men and women experienced in the promotion of talent, to examine the factors such as talent development, poor teaching methods, shortage of school accommodation and early entry into industry, which are responsible for loss of talent, and to study methods for fostering its development. Dr. Schairer believes that 10 per cent of all funds for educational and scientific development should be earmarked for the search for talent, including the earmarking of scholarship funds for the discovery and promotion of creative talent, especially in the age group 20–50. In this connexion, it may be noted that in a foreword to the recent pamphlet on "Teaching Mathematics in Secondary Schools", Mr. Geoffrey Lloyd said we had clearly reached a stage in which our methods and curriculum need to be considered afresh.

If the discovery of talent is a first priority, and the educational system of Britain should be constructed so as to ensure that, so far as possible, no school-leaver capable of benefiting by a university education should be debarred by lack of means from entering a university, it does not follow that room must be found in the universities for all who seek admission and have obtained the basic qualifications, whatever they may be. Creative talent is not necessarily best developed in a university, and if all real ability is channelled through the universities, the effects on various aspects of national life may well be adverse; quite apart from whether the nation can afford the necessary expansion in the resources devoted to university education. The expansion of university and technological education has clearly to be planned in some relation to the supply of appropriate talent; but it should also be in balance with the capacity of the educational system both to supply the supporting technicians and craftsmen needed for efficient use to be made of the most highly trained and creative man-power, and also to ensure that the general body of citizens has a lively appreciation of the issues involved. It is as vitally important to see that the main body of school leavers are adequately educated and able to face the demands of life in an age of rapid technological change, as it is to ensure that the best use is made of the brain-power available.

The recent White Paper on Secondary Education in Britain struck the right note in its emphasis on parity of opportunity, and the development of the educational system so that it can better produce citizens who are fitted by character, knowledge and skill to play their full part in an increasingly educated and responsible democratic society.

QUEEN AND SERVANT OF THE SCIENCES

Teaching Mathematics in Secondary Schools

(Ministry of Education Pamphlet No. 36.) Pp. viii+154. (London: H.M. Stationery Office, 1958.) 6*s*. net.

MUCH has recently been said and written about the claim that mathematics is a language, and in the foreword to this excellent volume (too valuable and too comprehensive to be termed a pamphlet), the Minister of Education himself asserts that the subject must be "taught as a language". Those who have made mathematics their special study will need no convincing that it *has* a grammar, a literature and a poetry. In the years before the Jeffery syllabus, which here receives critical examination and strong support, far too many boys and girls left school having spent a part of every school day working at 'maths' without being allowed (as was Moses) to gain even a glimpse of the Promised Land. In fact, they probably never knew that there was anything worth working for, anything but 'sums' and (worse still) 'problems'; they had all the drudgery of the driest of the grammar and none of the fun of the literature, much less the poetry. But for one limiting factor (to be mentioned below) this should no longer be the case for any of the teeming multitudes in the secondary schools of Great Britain, and the various chapters in this book set out clearly and enthusiastically why (and to some extent how) this can be accomplished. No authorship is, of course, ascribed to this official publication, but one thing is certain: 'they' have all taught the subject successfully, for only after experiencing the thrill of success with a class could these chapters have been written.

Every library in Britain should have copies of the book on its shelves, if only because it contains a valuable account of the development of mathematical teaching in England (and Wales ?) since the middle of the nineteenth century. A footnote (p. 67) reveals the authorship of the first official publication (Circular 711; 1909), which guided the schools in using the new-found freedom from the "bad parts of the Euclidean tradition". By the saddest coincidence, W. C. Fletcher (1865–1959) died two days before Pamphlet 36, which thus pays tribute to his great work for school mathematics, was published. All teachers of mathematics—not only those who dare to call themselves mathematicians—should read, mark, learn and inwardly digest this new book. In it they will find the encouragement to make themselves better able to teach, and the advice that the reports of the Mathematical Association provide the best means of doing this.

The rest of the volume gives an excellent outline of the present position (Chapter 2) in English secondary schools, goes on to show (Chapter 3) how essential it is to understand what has been done in the primary schools, and Chapter 4 discusses critically much of what is done (and should not be) in many secondary schools, as well as giving much sound advice on what should be done in the next four or five years. These years, which for the majority of boys and girls have no General Certificate of Education or any other examination at the end of them, will contain the only full-time instruction in mathematics these young people will receive. How essential it is, therefore, that the content and the approach (Chapter 6) should be the right one.

Chapter 5 is concerned with the sixth form, and emphasizes the risks we run if pure geometry receives less and less time and attention. Technique in the classroom, including comments on homework and marking (Chapter 8), and the relationship of mathematics to other studies (Chapter 7) are carefully treated, and the importance of an adequate background of the history of mathematics (Chapter 9), so that the teacher may weave a golden thread through all his lessons, is emphasized with appropriate examples.

The limiting factor in all this is, of course, the dire shortage of capable teachers, and without them the high ideals inspired by the report cannot be fully achieved. Yet even here there is cause for hope. "The fear of mathematics is more widespread than it should be", and "girls capable of going far in the subjects are more numerous than is commonly supposed" indicate that it should be possible to inspire a greater interest and facility in many more young people if "a real attempt is made to fit the mathematics to the pupil". Even with the present teaching staff, many of whom are gallantly attempting to teach up to the limit of their own accomplishment, much more can be achieved through the right approach and the best methods. By this means more boys, and especially more girls, may be encouraged to specialize in this subject, and so enable Britain "to remain in the forefront of scientific advance".

W. J. Langford

ATOMIC COMFORTS

On Nuclear Energy

Its Potential for Peacetime Uses. By Donald J. Hughes. Pp. xi + 263. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1957.) 30s. net.

This book represents one of the first attempts to combine an account suitable for the layman of the fundamental physical facts of nuclear energy with a discussion of its national and international implications, in particular of the possibility of development by peaceful international co-operation. In a foreword, Mr. Lewis L. Strauss describes one part of the book as being "one of the most complete and responsible surveys of the subject to appear in print". One fears the worst after this: fortunately, one's worst fears are not quite realized.

But in the chapter entitled "The International Atom"—even though the sub-section in question is headed "International Atomic Energy before Geneva" and the Geneva Conference on the Peaceful Uses of Atomic Energy was held in 1955—nothing is said of the period between 1945 and 1953. The year 1953, the first year of the Republican administration in the United States under President Eisenhower, is treated as the start of the period of international negotiation. Would it have been irresponsible to mention the diplomatic struggle of the first seven or eight years—the first half, indeed, of the atomic age ?

In a later chapter having a sub-section headed "Safety in Bomb Tests", the author takes two-thirds of a page to discuss whether to discuss this matter, then less than three pages to dispose of it. Although the dangers of radioactive strontium are mentioned (in two paragraphs), leukæmia is not, and no quantitative statement is made—even of the range covered by the (irresponsible ?) estimates of danger.

Perhaps the real difficulty is that all but about a third of this quite short book is devoted to the necessary layman's introduction to nuclear energy, with chapters headed "Fundamentals of Fission and Fusion", "The Chain Reaction", "Atomic Power", "Neutrons from Reactors", "Radioisotopes", and "Fusion". This part is competent, though undistinguished, but it leaves too little space for the rest, the chapters which the now educated layman must study before he can know what are the problems before him.

Dr. Hughes's repetitive and muddy style of American writing reduces further the amount of information which he can convey. To quote a few sentences out of context: "The destructive phases of fission and fusion energy are practically completely involved with their use as military weapons". "It is a matter of statesmanship to assure that man's life shall be enriched and not destroyed by the developments, rather than to halt a branch of research by edict." "It is interesting, however, that in both personal and information security the concept of negative and positive aspects just discussed plays an important role." Such a style makes clear thought difficult, and it is to be doubted whether the author could have steered us through the really controversial questions in his field. He mentions controversies which have arisen, but a little regretfully. On one question, that of security, he takes a forthright stand, pointing out the danger, even from the strictly national point of view, of too much "negative security".

The book does give a reasonable account of the status of the main national atomic energy projects, and is perhaps at present the best compact source of this information. On the whole, however, I find it too responsible, too comfortable, and too non-controversial. A determined and well-meaning layman who worked through it would scarcely know what all the fuss had been about. G. O. JONES

QUADRUPOLE RESONANCE

Nuclear Quadrupole Resonance Spectroscopy

By T. P. Das and E. L. Hahn. (Solid State Physics: Advances in Research and Applications, Supplement 1.) Pp. ix+223. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1958.) 7 dollars.

THE subject-matter of "Nuclear Quadrupole Resonance Spectroscopy" is the resonance phenomenon associated with transitions between states the energies of which depend on the interactions of the nuclear electric quadrupole moment with the field gradient provided by the environment of the nucleus. A small magnetic field may be applied in certain cases and its influence is then treated as a perturbation. The converse case of nuclear magnetic resonance in which the quadrupole effects may occur as a perturbation was dealt with in an earlier volume of this series.

The basic physics of the subject is now well understood and quadrupole resonance thus takes its place as an analytical technique of use both to the solid state physicist and the chemist. This book consists of about 80 pages of theoretical discussion, 10 pages on experimental technique and a little more than 100 pages on applications. The reader is referred elsewhere for a discussion of the fundamental theory, and the account of the applications is not claimed to be exhaustive; but in other respects the book is fairly complete.

One of the practical advantages of quadrupole resonance spectroscopy is that it may be carried out without the use of large and expensive magnets associated with nuclear magnetic resonance experiments. On the other hand, the apparatus employed must be made to tune through a very wide band of frequencies and it is therefore usual to use the damping of what is essentially a super-regenerative receiver as a means of detecting resonance. In such a system it is only necessary to vary one tuned circuit. The descriptions of several satisfactory circuit arrangements have been published and references are given.

The applications discussed in most detail are the determinations of the orientations of molecules in the unit cell and the study of the nature of bonding in various solids.

The work as a whole provides a valuable general introduction to the subject and is likely to be of particular interest to chemists. It is to be regretted that the proof reading was not carried out with more care. R. H. TREDGOLD

RATIONAL DISCUSSION

The Logic of Scientific Discovery

By Prof. Karl R. Popper. Pp. 480. (London: Hutchinson and Co. (Publishers), Ltd., 1959.) 50s. net.

IT is customary to believe that scientific method has been explained by Bacon and Mill once and for all. Yet science has changed greatly since these two men—who were not scientists—wrote; and so its methods must have changed as well. Einstein, in his Spencer Lecture given at Oxford in 1933, was the first to point out this change. We do not gain knowledge by reading 'the book of Nature' or by following 'a principle of induction'. We start, instead, by inventing a hypothesis and then proceed to test it by its consequences.

This hypothetical-deductive method was developed in detail by Prof. Karl Popper in the German version of the present book, "Logik der Forschung", published in Vienna in 1934. Pre-war conditions prevented the book from being easily accessible in the English-speaking world. Nevertheless, its ideas infiltrated, so that to-day there exists scarcely a philosopher or scientist who does not reject 'inductivism' and accept the hypothetical-deductive method.

The crucial experiment, according to Popper, is the means by which we decide whether or not to accept a hypothesis or theory. In such an experiment, like Michelson's, we try to falsify a hypothesis. If the outcome is positive, that is, if the singular statements derived from it have not been falsified, the hypothesis has withstood the test and is accepted. A hypothesis is never conclusively verified, for it is usually a universal statement; and no finite series of tests could ever establish its truth or falsity. Such a statement, however, is logically equivalent to a negative existential one, and this can be overthrown by a single experiment. Thus a hypothesis 'proves its mettle' or a theory is 'corroborated'. 'Confirmation', which is the common term describing this situation, is rejected by the author, for it suggests that we can firmly establish a hypothesis; and this is never so in science.

Another reason for rejecting induction is that it does not provide a criterion which would allow us to separate science from empty speculation or physics from metaphysics. This is, indeed, a basic problem, well known from the history of science: many attempts have been made to solve it. Physicists usually speak in this connexion of 'meaning'. Factual statements are meaningful if they can be tested by experiment, at least in principle. For example, statements referring to the simultaneous and exact values of position and momentum of a particle are meaningless in quantum mechanics, since they are ruled out by the uncertainty relations. Prof. Popper altogether rejects a criterion of meaning and replaces it by one of demarcation that is agreed upon by convention and "ultimately a matter of decision, going beyond rational argument". Indeed, what we accept as factual or real changes with the progress of science and is not decided by words; but a criterion of meaning could, in my view, do this job as well.

The more falsifiable a hypothesis is, the more it forbids, the more does it say about the world. This is the well-known inverse relation between logical range and factual content of a statement. The hypothesis which is falsifiable in a higher degree can also be corroborated better; and this depends less on the number of favourable instances than on the severity of the tests the hypothesis had undergone. The degree of falsifiability is complementary to logical probability which, however, must not be confused with numerical probability as we know it from statistics. According to Prof. Popper, statistics cannot help us in corroborating a hypothesis. His views on probability are highly controversial and, I fear, will not be readily shared by practising scientists.

The original text has been enlarged by footnotes and appendixes which make up more than one-third of the book. These additions do not help the book, not only because they are difficult to read, but because they are unduly polemical. A larger criticism is that physics is the only science talked about by the author. However, the rational discussion of its concepts—which Prof. Popper regards as "the one method of philosophy"—results in laying the ghost of induction, and this is the outstanding merit of the book.

E. H. Hutten

NATURAL HISTORY OF BRITISH SPIDERS

The World of Spiders

By Dr. W. S. Bristowe. (The New Naturalist: a Survey of British Natural History.) Pp. xiii+304+36 plates. (London: William Collins, Sons and Co., Ltd., 1958.) 30*s*. net.

ALTHOUGH an extremely widespread invertebrate group, spiders have for long been avoided by most British naturalists, amateur and professional. The reasons are probably straightforward: spiders have no æsthetic appeal to the amateur, as have, for example, Lepidoptera, beetles and dragonflies, while the professional has always regarded their biological importance as very low. None of the British species can be regarded as pests in any way, and although they must rank as one of the most important invertebrate predators, their choice of prey is to a great extent non-selective and no means have been found of using their activities to regulate harmful insects or in other ways. Until recently, their interest to the biologist has largely been academic, and the great names in the history of British araneology have been almost all taxonomists. To Dr. Bristowe must go the credit of rediscovering spiders for naturalists in Great Britain, not as lifeless pickled specimens, but as living creatures with activities and behaviour patterns of incredible diversity and quite as fascinating as any other invertebrate group. This book has an unrivalled wealth of personal observations on a great many different species of spiders, both captive and in the field, all of which have been made in his spare time during a busy professional life.

The first two chapters deal with two subjects which are characteristic of Dr. Bristowe's wide interest: spiders in literature and superstition, and what might be called a natural history of British araneologists. Together they form an excellent introduction to the main part of the book and will appeal to all naturalists whether they have a knowledge of spiders or not. Chapters 3 and 4 deal with structure, classification, and the fossil record. Chapter 5 touches all too briefly on the subject of population densities of spiders, and the influence of these numbers on other invertebrates. The next fifteen chapters describe and discuss the biology and behaviour of selected species of all the spider families represented in Great Britain.

While the character of the individual spiders is vividly portrayed by Dr. Bristowe, a less clear picture emerges of the ecology of spider communities. The book is, of course, concerned with the British fauna, but as studies on spider ecology are all very recent and include so much original work and new discoveries, some account of them would have helped to complete the picture. No reference is made, for example, to the excellent studies by Nørgaard in Denmark on the ecology of the *Pirata* species, of *Theridion saxatile* and *Lithyphantes albomaculatus*, all represented in Britain, nor to the population studies in Germany by Bochmann and Knülle on salt-marsh spiders, and by Tretzel and others on terrestrial habitats. A wide new field has developed on this subject during the past twelve years which shows excellent promise of narrowing the gap between our knowledge of spider ecology and that of better-known invertebrate groups.

There is a final chapter on collecting spiders, an up-to-date species list as an appendix, and a short bibliography.

One of the most impressive features of the book is the really excellent series of 332 drawings in line and wash by Arthur Smith. These were specially made for the book and immediately places this volume of the "New Naturalist" books in the front rank of the series for accurate and beautiful illustrations. Dr. Bristowe writes as an enthusiast in a fluent and very readable style. It will be no surprise if this book results in many converts to the study of spiders.

Eric Duffey

CARBOHYDRATES COMPLETE

The Carbohydrates

Chemistry, Biochemistry, Physiology. Edited by Ward Pigman. Pp. xvii+902. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1957.) 20 dollars.

FOR some years the Pigman-Goepp book on the "Chemistry of the Carbohydrates" has been the main reference book for carbohydrate chemistry. The book now under review is a complete revision with a considerable expansion of the earlier Pigman-Goepp. For this compilation the editor, Ward Pigman, has brought in no less than twenty specialists in the field to assist him. They have succeeded in adding two new chapters in addition to re-writing and bringing up to date all the previous chapters in the "Chemistry of the Carbohydrates". The vast increase in the volume of publications on carbohydrates is illustrated by the claim of the editor that references are given to no less than 4,500 individual articles. At first glance the book looks like a 'big brother' of any one of the current volumes of the "Advances in Carbohydrate Chemistry" published by the same press, but on closer inspection it is quite clear that much more detail has gone into the new individual chapters. These serve to make the book an excellent reference book which can be used in conjunction not only with the "Advances" but also with the older edition, which does contain some material eliminated from the present book.

The first three chapters, "Structure and Stereochemistry of the Monosaccharides", by Ward Pigman, "Occurrence, Properties, and Synthesis of the Monosaccharides", by John Sowden, and "Esters", by A. Thompson and M. L. Wolfrom, follow the conventional lines of the first book; they are, however, much more comprehensive and are now well developed, and references are given in an exhaustive fashion. The chapter on "Glycosides, Simple Acetals, and Thioacetals", written by M. L. Wolfrom and A. Thompson, again contains much of the material of the older edition, but gives a better account of the reactions of carbohydrates with aldehydes and ketones: this treatment is excellent. "Polyols, Alditols and Glucitols", written by R. L. Lohmar, jun., represents an extension of previous work and gives a most interesting account of this expanding class of sugar derivative. In addition, the related inositols come in for up-to-date treatment and the whole chapter is important and timely.

Another extension is the discussion of acids and oxidation products by John W. Green, where aldonic acids, aldaric acids, uronic acids, ascorbic acids, and so on are treated together. Most important, the section on oxidative reagents which are of special application in carbohydrate chemistry has been extended.

Ethers, anhydro-sugars and unsaturated derivatives are dealt with in some detail in a clear-cut manner by John C. Snowdon. A very welcome account, since the subject is growing rapidly every day, is that on nitrogenous derivatives written by Ward Pigman with specialist collaborators. The rapid growth of this subject is clearly demonstrated by the fact that no less than seventy pages are devoted to the different aspects of the sugars containing nitrogen. Another almost equally long chapter is that on oligosaccharides, carefully written by W. Z. Hassid and C. E. Ballou. The reader is brought up to date on enzymic synthesis of oligosaccharides in this chapter and modern advances in enzymic studies in this field are well illustrated.

An important and well-written chapter is that on the identification and quantitative determination of carbohydrates by Ray Noggle, though this could well have been placed at the beginning of the book. It is interesting because it includes some work on isotope procedure, including the synthesis and degradation of labelled sugars. The chapter on polysaccharides has been sub-divided into phyto- and microbial polysaccharides and animal polysaccharides. It has been cut down somewhat from the earlier publication and is perhaps the least praiseworthy in the book. This is because there has been a great attempt to put *multum in parvo*, so that a catalogue is now provided which, although it may serve to whet the appetite, appears to be somewhat stilted in the way it is written.

An attempt to introduce yet another classification of the animal polysaccharides with new terms adds but little to an already confused nomenclature. However, the account is well provided with references and will be important from the library point of view.

An excellent chapter on the photosynthesis and metabolism of carbohydrates is produced by Ray Noggle. This is very important and it well illustrates the rapid development in this particular field in the past few years.

Finally, there is a chapter on "The Carbohydrates in Nutrition", by Harry G. Day and Ward Pigman. This is most interesting, it is well written, and adds in more ways than one yet another chapter to the story of our carbohydrate chemistry.

Taken as a whole the book is an excellent one. It will be consulted by chemists, biochemists (academic and industrial), by medicals, and all students of chemistry. An enormous amount of effort has undoubtedly gone into the book and Ward Pigman is to be heartily congratulated on his efforts.

There are very few typographical errors and the style, well known in the "Advances in Carbohydrate Chemistry", is very acceptable. An important fact is that the modern Anglo-American carbohydrate nomenclature has been used throughout.

M. STACEY

ABORIGINAL ART

The Tiwi

Their Art, Myth and Ceremony. By Charles P. Mountford. Pp. 185+64 plates. (London: Phoenix House; Melbourne: Georgian House, 1958.) 65*s*. net.

THE aboriginal art of Arnhemland in Northern Australia is particularly rich in the variety of its forms, technical control and harmony of colour and design. Tools and materials are of the simplest: cave walls, bark, wood and cane; black pigment, red, yellow and white ochres; brushes made from bark; and fixatives derived from the sap of tree orchids or from a mixture of wax and honey. Most men can paint and carve but some are more skilled than others and acquire a reputation within their region. Nevertheless, all work within the same tradition, and no premium is placed on individuality and innovation.

We already have two monographs dealing with art in Arnhemland, one by Mountford (1956), and an earlier one in colour by Elkin and Berndt (1950). The present volume is concerned with the art of Melville Island, 14 miles to the west, where a distinctive style has been developed in the treatment of figured bark paintings, carved and painted burial poles, decorated bark baskets and ceremonial spears. As elsewhere in Australia, most of these objects are produced for a ceremony, and their value is of an especially sacred character in so far as they form an integral part of the rite, and portray in geometrical and naturalistic figures the supernatural beings and events occurring in myths. Mountford makes the point that Tiwi art is more highly formalized than that of the east and cannot be interpreted without the aid of the artist. The interpretations of the paintings reproduced in black-and-white in this book are recorded by Mountford; what he does not tell us is how far similar interpretations were or would have been offered by other adult men in the community. Nevertheless, it is valuable to have at least the artist's point of view; and this, along with the superb photographs, make the book a useful contribution to studies of aboriginal art.

From the anthropologist's point of view the book is disappointing in that both title and publisher's note are misleading. Mountford does not give us an analysis of all Tiwi myth and ceremonial, but confines himself to a description of the ceremonies of mourning and initiation witnessed by him and the myths associated with them. He omits to give an outline of the social organization, though a knowledge of this is essential for a full understanding of myth and ritual. He himself, as leader of the expedition, had little time for research, but he might have made use of material already published by field-workers and listed by him in his bibliography.

PHYLLIS KABERRY

La Disputa Leibniz–Newton sull'Analisi

(Enciclopedia di Autori Classici, 2.) Pp. 239. (Torino: Editore Paolo Boringhieri, 1958.) 1,200 lire.

THIS valuable little book contains the principal documents in the Newton–Leibniz controversy over the invention of the infinitesimal calculus, translated into Italian and briefly annotated by Dr. G. Cantelli. Of these, the most important is the long review (generally held to be by Newton himself) from the *Philosophical Transactions* of 1715, which sums up carefully, but decisively, in the author's favour. To present-day readers, however, the most interesting things in it are the incidentals. Thus Newton claims that his method of fluxions is more rigorous than Leibniz's theory of differentials, since "we can form no idea of infinitely small quantities". Again, Newton admits that the majority of the results in the "Principia" were obtained by his new analysis and only afterwards clothed in geometrical form. Finally, he goes beyond the limits of the controversy to attack his rival's natural philosophy. Between Newton and Leibniz lies "an enormous difference": the first proceeds only so far as experimental evidence leads and then stops, while the second is a slave to hypotheses which he blindly believes as eternal truths.

On the other side of the dispute Leibniz, from modest beginnings and courteous exchanges, gradually raises the stakes as his honesty and good faith are increasingly questioned by Newton's friends. Expressions of admiration for Newton's genius give place to complaints and accusations; the claim to independent discovery becomes an assertion of priority. Then his supporter, John Bernoulli, plays his trump card: if Newton had in fact discovered the calculus earlier, why did he not use it in the "Principia", which offered so many opportunities for its application? Instead, there is not a trace of analysis in the whole work. . . .

What are the rights and wrongs of the quarrel? The editor confesses that he is at a loss to say. It would be safer to maintain, with Wallis, a neutral position and ascribe the invention of the calculus to neither party but to the pioneers, above all to Cavalieri and Newton's own teacher Barrow.

L. Roth

Systematic and Experimental Studies on Protozoal Blood Parasites of Egyptian Birds

By Dr. A. H. Helmy Mohammed. Vol. 1: Pp. xi+166 (plates 1–6). Vol. 2: Pp. ii+167–298 (plates 7–13). (Cairo: Cairo University Press, 1958.) n.p.

THE book is the outcome of a survey, for protozoal parasites, of birds collected, near Cairo, over two complementary halves of two years, during which time some 885 birds were examined. It is, then, a report on the personal research of the author and serves, not as a general text-book but as a useful reference book for the limited few working in similar fields. Of necessity it varies in the accuracy of the incidence figures according to the methods of examination and to the numbers of a host species examined, and, in common with other works of this kind, does not claim to be complete.

The first section is devoted to speculations on the meaning of the figures for incidence listed early in the report; some are based on evidence too scanty to be of any practical importance; others, for example the use of evidence on distribution of the parasites to hint at the identities of their vectors, may be used profitably by future workers. This is followed by three sections dealing in turn with the species of Piroplasms, *Plasmodium* and *Haemoproteus*, found in the survey, together with reviews of the systematic problems surrounding these parasites. Dr. Mohammed includes sufficient information to clarify the problems in hand without attempting general reviews. The last section is an account of the development of *Haemoproteus columbae* in the pigeon fly, *Pseudolynchia canariensis*, a confirmation and extension of the work of H. Adie in 1915.

Elizabeth U. Canning

A Guide to Field Biology

By John Sankey. Pp. xvi+166. (London and New York: Longmans, Green and Co., Ltd., 1958.) 12*s.* 6*d.* net.

IT is particularly appropriate that the author of this admirable little book should be a warden at one of the centres of the Field Studies Council, which has played a notable and pioneer part in encouraging field biology in secondary schools in Britain. As might be expected of one with ten years experience in this type of teaching, Mr. Sankey's account is lively and practical in outlook. Ecology is a subject which is not easy to teach or to write about. The simple and straightforward approach adopted in this book should go far towards dispelling any doubts, still often voiced in educational circles, that field-work is too complex to be undertaken profitably without elaborate apparatus and a disproportionate expenditure of time. Guidance is given on how to study particular kinds of plant and animal habitats and there are useful sections dealing with such aspects as the planning of projects, also methods of collecting and identification.

W. H. Dowdeswell

Venture to the Arctic

Edited by R. A. Hamilton. (Pelican Book No. A432.) Pp. 283+32 plates. (Harmondsworth, Mddx.: Penguin Books, Ltd., 1958.) 5*s.*

THIS book performs a new and very welcome function in the sphere of expedition literature. It tells, in terms of popular science, the story of the British North Greenland Expedition of 1952–54. The main narrative of any expedition, normally written by the leader, cannot find room for more than a few pages on this, and anyway, is almost always written before the results are known; and the results themselves are both too technical and scattered over a wide range of journals. This book is directed to the 'man in the street', who is entitled to hear about what he has helped to pay for. He will find it of fascinating interest, and his idea of what a modern scientific expedition accomplishes will probably be considerably extended. But although it is designed for the non-specialist, the contributors have rightly understood that popularization implies simplification of language rather than of ideas, so that the specialist will also gain from reading it. R. A. Hamilton, as chief scientist, fills in the background of planning and organization, and contributes his own meteorological results, besides editing the whole. F. R. Brooke describes the survey, C. B. B. Bull the seismic sounding and gravity work, J. P. Masterton and H. E. Lewis the medical and physiological aspects, H. Lister the glaciology, J. D. Peacock the geology and P. J. Wyllie the geomorphology. It is much to be hoped that other expeditions will follow this lead. They could have no better example before them.

T. E. Armstrong

THE ZOOLOGICAL SOCIETY OF LONDON

By Sir SOLLY ZUCKERMAN, C.B., F.R.S.
Secretary, Zoological Society of London

OVER the past eighteen months the affairs of the Zoological Society of London have attracted considerable attention in the national Press, first because of a proposal to alter the Society's by-laws, and more recently through the publication of plans for the reconstruction of the Regent's Park Gardens. Alterations in the Society's by-laws can be proposed only by the Council; but the constitution demands that they have to be endorsed by the body of Fellows. The 1958 proposals, one of the main objects of which was the strengthening of the scientific and educational activities which are the sole purpose for which the Society was incorporated by Royal Charter in 1829, were accepted by well over half the 3,000 Fellows who took the trouble to vote. One of the dissenting minority decided to challenge the Council on the construction of the by-law defining a majority, his argument being that in order to validate any proposal about by-laws it was necessary to obtain an absolute majority of the 7,000 or so Fellows in the Society, whether or not they voted. This view was upheld in the Chancery Division on December 5, 1958, but reversed in the Court of Appeal on March 20, 1959.

To see this affair in perspective, it is useful to consider the past history of the Society; its future plans; and the purpose of the 1958 changes in the by-laws, which have now become effective.

History of the Society

The Society was founded by Sir Stamford Raffles and Sir Humphry Davy, then president of the Royal Society, "for the general advancement of zoological science". As an immediate object it was hoped to collect in London "such living species of the animal kingdom as may be introduced and domesticated with advantage in this country". It was also suggested that the Society should found both a zoological museum and "a Library of all Books connected with the subject". The first problem was to find the money necessary to realize these objects, as well as the authority to establish a menagerie on Crown land in Regent's Park. Almost inevitably the Fellowship became a combination of professional zoologists, and of subscribers who ranged from amateurs with a deep specialist knowledge of a particular part of zoology, to persons to whom membership was little more than a means either of granting patronage or, in some cases, of gaining prestige or privilege. There was no alternative to this development if the resources were to be found.

After considerable negotiation with the Government, a lease of five acres of Regent's Park was granted in 1826, which was soon increased to about thirty acres. Within ten years there were 3,000 Fellows, and for the first twenty years or so entrance was restricted to them and their friends, since they, in effect, were the patrons whose contributions had made the venture possible. Their number then started to decline, and in 1847 it was decided to admit the public by payment at the gates. The reason for this departure was essentially financial, even though the Council of the day was authorized to express the Crown's approval of the step as a measure which helped to diffuse "intellectual recreation among the great mass of the people". The decision brought an immediate improvement in the Society's fortunes. Within three years total revenue had all but doubled, and Fellows' contributions fell to about 40 per cent of a budget of about £15,000. In 1900 incomings were about £29,000, to which Fellows contributed about 38 per cent. By 1938 the proportion had fallen to 16 per cent, and to-day it is only about 5 per cent of the half-million pounds a year now needed to administer the collections of animals in Regent's Park and in Whipsnade Park, nr. Dunstable, Beds, and the Society's many other activities.

The spark which touched-off the recent dispute in the Society's affairs was a decision by the Council to open the Regent's Park Gardens to the public on Sunday mornings, which *ipso facto* meant the withdrawal of a privilege of restricted entry which was highly valued by some Fellows. One of the main reasons for this decision was the Society's urgent need for funds to meet rising costs and to start a major rebuilding programme. Sunday afternoons, which had been 'public' since 1940, already provided through gate receipts relatively more to the Society's revenues than the takings of any full day of the week. Additional receipts on Sunday mornings over this past year have practically equalled the total net revenue received from Fellows. The question of rates was the second main reason for the decision to open the Gardens. The Council had been advised that only a substantial increase in the amount of voluntary subscriptions, and a decline in the proportion of the subscriptions from which the Fellows derived a personal benefit, would make it possible for the Society to qualify for exemption from liability to rates as a scientific society under the Scientific Societies Act of 1843. The withdrawal of the privilege of exclusive entry on Sunday mornings has already materially altered the situation.

The uproar this occasioned did not come from the hard core of professional zoologists who are members of the Society. For many years there appears to have been an attitude within the administration of the Society that all subscriptions to its coffers were to be welcomed, whatever their source. As a result, the Fellowship of the Society has at times risen to as many as 8,000, and it is not surprising, therefore, that some of those who became Fellows were unaware of the fact that the existence of the Zoological Society as an institution under a Royal Charter depended solely on the fulfilment of the object for which it was founded—namely, the advancement of zoology and animal physiology. Attitudes resulting from a confused interpretation of this purpose are undoubtedly to blame for some serious public misunderstandings about the nature of the Fellowship.

Scientific Activities of the Society

But however prevalent the misunderstanding, the Society has at no time failed to discharge the obligations of its charter. The Library which was started in 1835 is now one of the finest collections of zoological literature in the world. A Museum begun even earlier provided a valuable part of the early collections of the British Museum (Natural History). Regular scientific meetings have been held uninterruptedly ever since 1827, the Society taking over from the Zoological Club of the Linnean Society, which was then dissolved, as a national forum for zoological discussion. The leading zoologists of Britain have always contributed to these meetings, some of which, for example the famous meeting which in 1919 considered the phylogenetic and taxonomic status of *Tarsius*, are part of the general history of zoological science. The *Proceedings* of the Society, which now appears eight times a year, began in 1830, and the first part of the *Transactions* of the Society appeared in 1833. Both have been issued uninterruptedly ever since. Since 1886, the Society has also been responsible, for a time in association with the Royal Society, for the publication of the "Zoological Record", which had been started in 1864 by a group of zoologists connected with the British Museum.

In addition to this normal pattern of discussion and publication, which applies to all scientific societies, the Zoological Society has always been somewhat more directly concerned with the advance of zoology both through the work of its officials, and through the provision of anatomical and pathological material to research workers in other institutions. This contribution appeared more conspicuous in the nineteenth and earlier part of the present century, when the total volume of zoological research was far less than it is to-day, and when its emphasis was largely morphological and taxonomic. With the recent establishment of a new Veterinary Hospital and Pathology Department, the standards of animal husbandry in the Society's menageries, as measured by the decline in mortality-rates and an increase in birth-rates, are now improving fast. To-day both indices stand at record levels in the Society's history. The provision of new laboratory facilities will undoubtedly strengthen the direct part which the Society can play in the future advance of zoological science.

Educational Activities of the Society

These activities represent one of the two ways in which the Society discharges its obligation to advance the science of zoology. The other is the encouragement of zoological education, primarily, of course, through the maintenance of animal collections which, excluding fish and invertebrates, to-day constitute nearly 1,200 species or subspecies. The Society's menageries provide a far better picture of the range of the animal kingdom than, so far as is known, any other zoological collection in the world.

In co-operation with the educational authorities of the Greater London area, and with the help of the Nuffield Foundation, the Council, two years ago, established regular courses for school-children up to and including the sixth form. These have proved very popular, and a number of schools are now including the lecture-demonstrations as a normal part of their teaching time-table. In the previous year, the Society had established, jointly with the Granada T.V. Network, a full-time Television and Film Unit, the main effort of which now is the preparation of a series of films representing different aspects of animal life. This venture should add greatly to the Society's educational potential, as will also a Young Zoologists Club, founded early this year, and which has already attracted more than 1,300 members.

New Subscription Rates

The Council is confident that the reform in the structure of the Society made possible by the new by-laws will not only lead to an increase in the net revenue from Fellows, but will also powerfully reinforce the scientific strength of the Fellowship. Until this year the subscription of a Fellow had remained unchanged at £3 for well over one hundred years, and was incommensurately low in relation to privileges which potentially could be demanded in return. But unlike what prevails in almost every other scientific society, a Fellow did not obtain the published *Proceedings* of the Society as of right. Many professional zoologists who were unable to attend meetings, and who were uninterested in other rights of subscribers, could scarcely, therefore, see how membership helped develop their own science. Equally, they found it difficult to see how in such circumstances they could assist the Society in achieving its purpose. Raising the subscription of Ordinary Fellows to a realistic level had, therefore, to be reconciled with the certainty that very few scientists or teachers would belong to the Society at all if their subscription was not kept within the normal range of other scientific bodies. The 1958 by-laws have achieved the necessary compromise. Scientific Fellows now subscribe £4 and receive the *Proceedings*; while Ordinary (non-professional) Fellows subscribe £8 a year, without receiving the Society's scientific publications. Non-voting Associates continue to pay the old 1832 subscription of £3. While not deterring non-professional patrons of zoology, these changes will, it is anticipated, lead to a powerful recruitment of professional research workers and teachers of zoology.

Building Plans

By coincidence, the decision of the Appeal Court that these changes in the structure of the Fellowship had been validly confirmed by the Society was announced almost simultaneously with the publication of plans for the rebuilding and re-landscaping of the Regent's Park Gardens. The main purpose of the new plans, which have been devised by Sir Hugh Casson and Mr. F. A. Stengelhofen, is threefold. First, they provide modern accommodation for the animals; secondly, they improve public amenities and facilitate the circulation of visitors; and thirdly, they improve the Zoo æsthetically, by a more spacious and yet cohesive lay-out. The pre-requisite of a flexible master-plan was the need to achieve an initial degree of mobility by clearing at least one big site in an already overcrowded area. This will be accomplished in about a year's time, when the building of a new Works and Supplies Department, which is now being erected, is completed. The area at present being occupied by the Works Department will then be developed as paddocks for deer and antelopes, and the present quarters of these animals will in turn be adapted for elephants. From then on the plan should unfold smoothly.

The first step in planning was, of course, to define a general policy about animal collections. The decision was that a zoo in the metropolis should avoid expensive duplication and should contain, for educational purposes, as representative a series of the more important types of animal as can be got together. The aim, therefore, is to have in Regent's Park a collection the value of which is measured not by the number of its individual exhibits, but by the extent to which it represents the animal kingdom. In achieving this policy, the Society has the enormous advantage that since 1931 it has also owned Whipsnade Park, which covers more than 500 acres, and where the Society can help play a part in projects of animal conservation, such, for example, as keeping in existence species (for example, the Père David deer) that have already disappeared in the wild.

While these and other basic considerations were in process of decision, detailed consultations were started with the Ministry of Works and the Commissioners of the Crown Estate, who are the Society's landlords in Regent's Park. The new plan not only has their general approval, but also that of the London County Council and the Royal Fine Arts Commission. The larger part of the Zoo is on the south side of the Outer Circle. The main gate by which it is entered is being moved in such a way that the visitor of to-morrow will see down broad steps into a 'square' from which he can look around the Zoo and also into the Park beyond. At the same time, the Zoo and the Park will be landscaped so that their natural features are continuous on either side of a water-barrier which will mark the boundary between the two. Within the Zoo different areas will have distinctive characters, and will be connected by elevated walkways. The north gate will be moved to a more central position near a new bridge, and the banks of the canal, which separate the north from the middle garden, will be used, wherever possible, as grazing paddocks. The scientific and educational buildings will also be increased in size.

Fortunately, the first three years of rebuilding can be paid for out of funds which accumulated during the post-war period, when building restrictions made it impossible to carry out any reconstruction, and when large crowds visited the Regent's Park Gardens partly because of restrictions on motoring, and partly because of the relative lack of other public attractions. But in due course new sources of revenue will have to be found. The Society does not get any subsidy from public funds, except indirectly, in so far as the rent it pays for the Crown land it occupies has not increased for more than a hundred years. Almost every other big national or civic zoo in the world is subsidized. For example, the New York Zoo receives annually from the New York municipal authorities a sum that almost equals the total revenue which the Zoological Society of London has to earn. Other American zoos are also supported by their city governments. Most of the German zoos are municipal zoos which were reconstructed after the War out of public money. The Paris zoo depends for support on the Ministry of Education. The complete fulfilment of the plan for the Regent's Park Gardens will almost certainly need sources of revenue additional to that provided by the public at the gates.

Wherever the money comes from, the present plan of rebuilding is not some visionary scheme for an undefined future. It is a programme of redevelopment that is already being pursued. It is a plan, too, the implementation of which coincides with the first major change that has been made in the structure of the Fellowship since the Society's foundation 130 years ago. This change re-emphasizes the scientific and educational purpose for which the Society exists. In 1841, when the Regent's Park Gardens were managed largely as a private venture for private enjoyment, the following resolution was passed at a general meeting by an overwhelming majority: "The Society cannot divest itself of the scientific character so essential to its dignity and respectability without violating the Charter of Incorporation". The sense of this resolution is far truer to-day, when the management of the Society constitutes a trust that can be vested only in those who have the necessary knowledge to discharge the scientific and educational purposes of the Charter, and also the official or business standing commensurate with the responsibilities which the Society carries on behalf of the public.

SHOREWARDS UPSLOPE OF THE LAYER OF MINIMUM OXYGEN OFF BOMBAY: ITS INFLUENCE ON MARINE BIOLOGY, ESPECIALLY FISHERIES

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Earlier Knowledge of Upwelling in the Arabian Sea

THERE are two factors of particularly great interest in the Arabian Sea: the seasonal upwelling caused by the prevailing monsoons and their changes, and the well-developed tropical subsurface layer of minimum oxygen. Both have pronounced effects on marine biology and especially on the seasonal nature of the local fisheries.

Upwellings along the Somali and South Arabian coasts and also around the southern tip of Ceylon during the south-west monsoon were indicated by Schott[1] on the basis of low surface temperatures then prevailing there. Upwelling could be expected to exist along the Bombay continental shelf during the north-east monsoon, and Jayaraman and Gogate[2] have earlier found indications which probably attest such between 20° and 22° N. latitude along this coast. Their conclusion was also based on the distribution of temperature and salinity there.

Layer of Minimum Oxygen

The tropical subsurface layer of minimum oxygen in the Arabian Sea has been described in reports devoted to the *John Murray* expedition of 1933–34. Of all tropical seas the layer of minimum oxygen is most pronounced in the Arabian Sea, where the oxygen content is nearly nil at its mid-depth. The upper boundary of the layer is relatively sharp and coincides with the sharp thermocline or is slightly below it. The depth of the thermocline varies seasonally, dependent upon the seasonal upwelling or the coastal piling-up of the surface waters according to the prevailing monsoon. According to Schott[1], the layer of minimum oxygen is most pronounced off Bombay, where it is found generally at the depth of 50 metres.

Most usually it is found in the northern part of the Arabian Sea at the depth of 75 metres, but towards the equator it descends to reach a depth of about 150 metres. Salinity within the layer is relatively high, being in the north around 36 per mille and in the central Arabian Sea about 35·5 per mille with temperature at 22–23° C. It is noteworthy that the salinity maximum is found slightly below the layer of minimum oxygen. Gilson[3] found a high nitrite content in the layer of minimum oxygen, and immediately above it a high concentration of plankton was recorded.

The layer in question cannot fail to have a pronounced effect on marine life. It is to be expected that where it runs into the contour of the continental shelf, very little if any animal life will be possible beneath. Furthermore, in the event of upwelling raising the layer of minimum oxygen, animal life in the water above will be endangered. Proof of this has been recorded on several occasions. There is an area in the southern part of the Arabian Sea, between long. 60–65° E. and lat. 6–12° N., where mass mortalities of pelagic fish have often been reported during the month of June. This area being a divergence area of winds and of the drift currents caused by them (it is actually the centre of a gyral), upwelling of the layer of minimum oxygen there is to be expected. Mass mortality of fish has also been reported along the Arabian and Indian coasts in areas and seasons where and when upwelling of the layer is to be expected. Such mass mortalities might very well be caused by the upwelling of the layer of minimum oxygen alone or in conjunction with the accompanying 'red tides'.

Investigations off Bombay during October–November 1958

Some modest investigations were made off Bombay during the latter part of October and the beginning of November 1958 by the personnel of a refresher course in marine biology sponsored by the United Nations Educational, Scientific and Cultural Organization. Because the north-east monsoon starts in October, an accompanying upwelling of the layer of minimum oxygen along this coast should be expected then because of the direction of the wind. This was in fact found, the layer with an average oxygen content of 0·7 ml./l. occurring at an average depth of about 18 m. some 18 nautical miles out from the coast. The slope of the discontinuity layer was upwards towards the coast (Figs. 1–3). The salinity in this layer of minimum oxygen was about 36·0 per mille and the temperature around 24° C. The phosphate content was also relatively high (greater than 1 µgm. at./litre). In a zone 7–10 nautical miles from the coast, the layer of minimum oxygen practically reached the surface. The oxygen content there was very low from surface to bottom (see Station 4). An intensive mixing by tides takes place in this zone, where the water was found to be rather turbid. Inshore of it there was coastal water which was also thoroughly mixed by the tides and which contained higher amounts of oxygen. This coastal water was extremely muddy because of the intensive tidal mixing and the soft nature of the bottom. Pronounced colour changes were noticed in the water. Near the coast it was brownish grey out to about 7 miles offshore. Seawards of this for some 3 miles the hue was greenish-grey. Still farther out the colour of the water graded into blue. Because the effects of the upwelling in

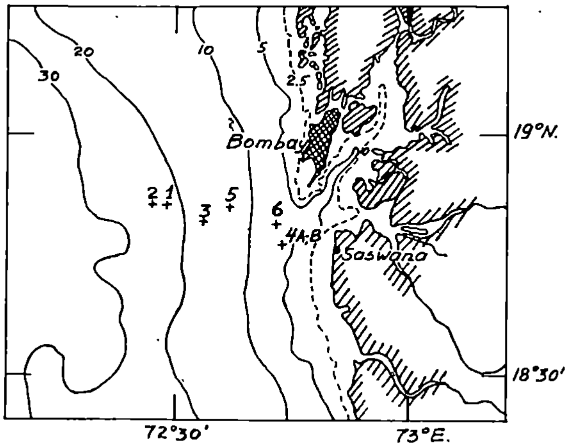

Fig. 1. Depth contours (in fathoms) and position of stations off Bombay

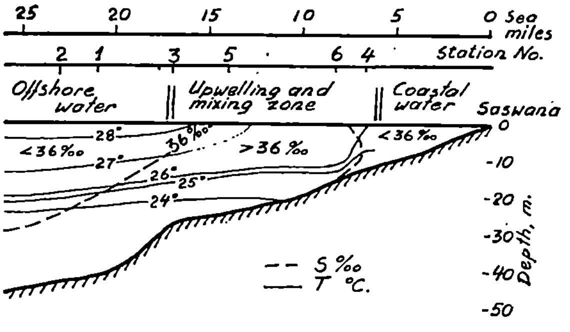

Fig. 2. Distribution of temperature and salinity off Bombay (beginning of November 1958)

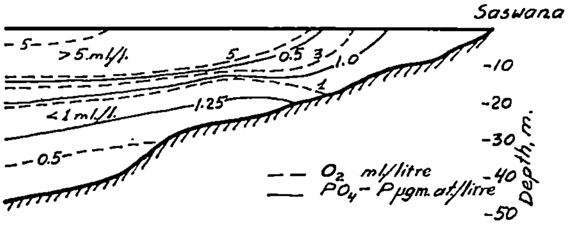

Fig. 3. Distribution of dissolved oxygen (ml./l.) and phosphate phosphorus (µgm. at./l.) off Bombay (beginning of November 1958)

respect of high salinity and high plankton production were detectable as far out as our Station 3 (17 miles offshore), the 10-mile-wide belt of water outside Station 4 (itself 7 miles from the coast) could be regarded as the 'upwelling and mixing zone'.

The layer of minimum oxygen shallows up the continental slope and intersects the bottom at about 7 fathoms depth. In consequence, demersal fish are forced to migrate shorewards during the upward movement of the layer. This results in notable concentrations of fish during the period October–December between the 'upwelling and mixing zone' (see Fig. 2) and the 'coastal zone' at about 13 miles out from Bombay harbour, that is, about 7 miles offshore from Saswan along the line of stations. Seawards of the upwelling and mixing zone there was a warm surface layer with relatively high phosphate and high oxygen contents. The upper boundary of the layer of minimum oxygen seems to rise and fall with the tides (see the observations from Stations 4*A* and 4*B* in the accompanying tables). This can be expected to cause up-and-down migrations of the fish concentrated in the area where the layer of minimum oxygen intersects the bottom contour. These vertical fish movements are known to the local bag-net fishermen. An abundant growth of plankton was found in the 'upwelling and mixing zone' which is likely to exhaust the nutrients from the surface layer rather quickly, and in fact a decreasing phosphate content was found going offshore. Also the oxygen content of the upper surface water showed a decrease farther offshore, which might be ascribed to the consumption of oxygen due to the decomposition of the organic matter produced in the upwelling and mixing zone and in its vicinity. Both the decrease of nutrient content in the surface layer and the downwards sloping of the thermocline and layer of minimum oxygen will probably continue as one goes farther offshore. Gilson[3] found in December and January off Bombay (at the edge of the continental slope) that the thickness of the surface layer was 50–60 metres and that it was completely depleted of nutrients.

The bulk of the standing crop of plankton was found above the discontinuity layer. The main phytoplankton organisms were: *Coscinodiscus*, *Trichodesmina* and *Ceratium* species. Of zooplanktonts the chief were copepods and sagittas. Scarcely any benthic animals were found in the depths where the oxygen content of the bottom water was less than 0·5 ml. per litre. In shallow water, benthos consisted mainly of hermit crabs, *Jibia curba* shells and a few nereid and polychaete worms.

The seasonal upwelling and the associated up-and-down movement of the layer of minimum oxygen caused by the changing monsoons have various important effects on the local fisheries. During the south-west monsoon the surface mixed layer will be rather thick and the layer of minimum oxygen correspondingly deep in the water off Bombay due to the piling up of surface waters. During the north-east monsoon the layer of minimum oxygen will gradually ascend into shallower depths because the surface waters will be blown seawards, so causing upwelling from below. The demersal fish which were distributed during the south-west monsoon over a large area on the relatively shallow continental shelf off Bombay will have to move into shallow water to escape lethal low-oxygen conditions. This chain of events will lead to the occurrence in shallow water during the north-east monsoon of fish concentrations easily available to the local fishermen and, in fact, there was a glut of landings soon after the start of the north-east monsoon in 1958.

Depth of sample	Temperature (°C.)	Salinity (per mille)	Phosphate phosphorus (μgm. at./l.)	Dissolved oxygen (ml./l.)
STATION 1. I.N.S. *Ranjit*. October 24, 1958 Lat., 18° 51′ N.; long., 72° 29′ E.; depth, 42 m.				
Surface	28·5°	35·35	0·39	—
9 m.	28·1°	35·70	0·43	5·21
22 m.	24·0°	36·45	1·25	0·67
STATION 2. I.N.S. *Madras*. November 4, 1958 Lat., 18° 51′ N.; long., 72° 27′ E.; depth, 43 m.				
Surface	28·0°	35·66	0·45	2·90
5 m.	27·8°	35·86	0·40	5·11
15 m.	26·5°	35·95	0·53	3·00
25 m.	23·4°	35·99	1·20	0·87
32 m.	23·4°	36·13	1·25	0·68
39 m.	23·2°	36·04	1·35	0·45
STATION 3. I.N.S. *Madras*. November 4, 1958 Lat., 18° 49′ N.; long., 72′ 34′ E.; depth, 26 m.				
Surface	28·2°	35·37	0·42	5·12
STATION 4*A*. Fishing vessel *Machwa*, KRJ 478. November 9–10, 1958 Lat., 18° 47′ N.; long., 72° 44′ E.; depth, about 14 m. Start of rising tide				
Surface	26·5°	35·88	0·93	2·6
5 m.	25·3°	35·91	1·09	1·75
10 m.	25·2°	(36·02)	1·06	1·25
12·5 m.	25·2°	35·91	1·09	1·2
STATION 4*B* (same as Station 4*A*). End of rising tide				
Surface	27·0°	36·22	0·56	1·25
5 m.	25·7°	36·17	1·09	1·20
10 m.	24·8°	36·04	1·13	1·4
12·5 m.	24·7°	35·82	1·16	0·5
STATION 5. I.N.S. *Madras*. November 11, 1958 Lat., 18° 51′ N.; long., 72° 37′ E.; depth, 25 m.				
Surface	27·0°	36·26	0·33	5·2
4 m.	26·9°	36·24	0·40	4·94
5 m.	26·55°	36·33	0·83	5·11
10 m.	26·25°	36·27	0·86	3·42
13 m.	24·85°	36·36	1·06	0·97
15 m.	24·4°	36·36	1·20	0·86
20 m.	24·4°	36·42	1·25	(1·00)
STATION 6. I.N.S. *Madras*. November 11, 1958 Lat., 18° 49′ N.; long., 72° 44′ E.; depth, 12 m.				
Surface	26·8°	36·26	0·71	3·30
5 m.	26·5°	36·24	0·86	3·14
8 m.	26·1°	36·11	1·31	4·29
10 m.	26·1°	36·09	0·71	3·03

The upwelling during the north-east monsoon causes also a high production of plankton off the Bombay coast, because nutrient-rich water is brought close to the surface, and it is naturally expected that pelagic fish would migrate into this area to feed on the rich standing crop of plankton then existing there. However, *Rastrelliger*, tunas, and Indian oil sardines do not come close to the coast in the Bombay area. It seems that these pelagic fish remain outside the 'upwelling and mixing zone' because of the low oxygen content of its water. Schools of pelagic fish were in fact sited at about 25 nautical miles off Bombay at the time to which this report relates.

The origin of the layer of minimum oxygen in the Arabian Sea is not yet fully understood, but it is associated with high salinities and relatively high temperatures, and several authors believe that it originates through the outflow of the Red Sea and Persian Gulf waters.

The seasonal behaviour of the surface layers of the Arabian Sea is not fully known. It would also be interesting to know the changes in intensity of the upwelling off Bombay during the north-east monsoon. From January onwards, the north-east monsoon turns along the Indian Coast to north and north-west. This turning might cause considerable changes in the conditions to be found during October–November and described above for the period here concerned.

Currents

Very obviously it would help greatly in the understanding of the oceanographical situations discussed above if it were possible to make observations of the speed and direction of the bottom water movements at regular and frequent intervals around the clock—say, every half-hour for a lunar day on a number of separated occasions. We had certain suitable apparatus of great simplicity for making such current observations, but time did not serve. Only a few spot observations were possible using the very simple instruments developed by one of us (J. N. C.), but a notable current one-third knot in speed was measured running towards about 210° magnetic. This was at the position lat. 18° 51′ N., long. 72° 29′ E., and served to show at least that the bottom water was not setting constantly towards the coast at the time. Perhaps it might have been found to set dominantly shorewards later after the north-east monsoon had become more strongly established. If so (and the matter should certainly be investigated), a mechanism explaining the shorewards uptilt of the layer of minimum oxygen would be to hand.

We wish to thank the participants in the refresher course in marine biology who were engaged in the collection of the observations; the Indian Navy for the provision of shipboard facilities, and Mr. K. Koli, who kindly allowed us to use his boat.

[1] Schott, G., "Geographie des Indischen und Stillen Ozeans" (Boysen, Hamburg, 1935).

[2] Jayaraman, R., and Gogate, S. S., *Proc. Ind. Acad. Sci.*, **45**, 151 (1957).

[3] Gilson, H. C., "The Nitrogen Cycle", Rep. John Murray Exp., **2** (2), 21 (1937).

RUSSIAN CONTRIBUTIONS TO THE INTERNATIONAL GEOPHYSICAL YEAR

THERE are eighty-six scientific institutions in the Soviet Union taking part in the programme of the International Geophysical Year. They are organized by eighteen departments and ministries of which the most important are the Academy of Sciences, the Northern Sea Route Administration, the Hydrometeorological Service, and the Ministries of High Schools and Communication. The Soviet International Geophysical Year Committee publishes regularly an Information Bulletin giving details of the Russian investigations. It has also issued a bibliography of International Geophysical Year publications, arranged the issue of a series of commemorative postage stamps, and is preparing a full-length popular scientific film in colour dealing with its contributions to the International Geophysical Year.

Antarctica

Particular attention has been given to Antarctic research. The Academy of Sciences set up an Antarctic Expedition in 1955 and has established three main stations: Mirny (near Haswell Island), Vostock (near the south magnetic pole), and Sovietskaya (near the pole of relative inaccessibility). The two inland stations are more than 1,400 km. from the coast. There are also at present three further research bases. The Mirny Observatory carries out regular observations in nearly all the fields of the International Geophysical Year programme, such as meteorology, glaciology, oceanography, geomagnetism, ionospheric physics, seismology, and the study of cosmic rays and of Earth currents. The other stations are run on more modest lines.

A magnetic profile was made from Mirny to Pionerskaya, and from this the existence of a mountain ridge under the ice 250 km. from the coast was inferred. This was confirmed by seismic and gravimetric investigations, which showed that the ice is 2,500 m. thick in some places, and that substantial parts of the ground beneath the ice are below sea-level.

It was established that the Antarctic ice cap is shrinking, like that of the Arctic, but at a very much slower rate. The variation of temperature with depth in rocks was investigated, and in certain inland regions they were found to be frozen (that is, below 0° C.) to a depth of 200–300 m. Frozen rocks were found to thaw to depths of 0·1–2·0 m. in summer.

Geologists studied the coastal region between 80° and 110° E. Exposed rocks are scarce there, and mainly old pre-Cambrian crystalline schist and gneiss, intersected by vast granite intrusions, were found. This confirms the theory that this region is part of a shield. Metamorphosed sands and conglomerates were also found in this region.

An air survey was made of the coastline between 40° and 166° E., and maps have been published of this area. Three expeditions studied ocean currents, using the electromagnetic methods of measurement, and sedimentation and bottom structure, in a large part of the Antarctic Ocean.

The Arctic

In the Arctic, too, there has been a great deal of activity, particularly on the drifting ice stations. It was found that in summer, atmospheric pressure is abnormally low in the central Arctic and this disrupts the normal ice drift. It was also found that the ozone concentration is very great in March. A comparatively deep marine trench (up to 3,000 m.) was found between Greenland and Spitsbergen, which is of importance in the flow between the central polar basin and the North Atlantic.

Oceanography

The non-magnetic ship *Zarya* voyaged extensively (including a trip from Leningrad to Indonesia, crossing the Atlantic six times and visiting Australia via

Cape Town), and found anomalies even in the deep ocean, and determined the present position of the magnetic equator. The oceanographic ship *Vityaz* spent much time in the Pacific studying currents. It determined the boundary of the sub-arctic front between the Kuroshio and Oyashio currents, of the subtropical front between the Northern Trade drift and the North Pacific drift, and of the north (and south) tropical fronts between the Northern (and Southern) Trade drifts and the intertrade back drift. It found velocities of as much as 10–12 cm./sec. at 1,000 m. in certain places (instead of an anticipated maximum of about 3 cm./sec.). A new trench was found north of the Fiji Islands, and a part of the Marianas Trench was found to have the record depth of 10,990 m. Photographs of the ocean bottom were taken at depths of up to 9,800 m.

Rockets and Earth Satellites

By June 1, 1958, three satellites had been put into orbit and fifty-nine rockets fired, including one which reached a height of 473 km. From readings transmitted by the rockets the air pressure up to 260 km. was determined—at 260 km. it is of the order of 10^{-7} mm. mercury. A mass-spectrometer was taken up and it was found that, between 105 km. and 206 km., the main ions present have a mass number 30 (which is interpreted as NO ions). Dispersion interferometers were also taken up to measure the electron concentration in the ionosphere. It was confirmed that there is no clear layer at an altitude of about 110 km. but merely a region of maximum concentration of electrons. Beyond this the concentration of electrons falls slightly, and then increases to the *F*-layer, beyond which, contrary to the American observations, only a slow decrease was found. Animals were sent up in some of the rockets. They were recovered by parachute, and some of the animals made many trips. In the second satellite an animal was carried, and was found to behave normally in a state of free fall, and to manage well with other peculiarities of cosmic flight, during the week in which the air-regenerating apparatus was functioning. Ionospheric measurements made with the satellites confirm the results obtained with rockets. Observations of cosmic rays were obtained by means of the satellites; their intensities differed from the predictions of the present theories about the Earth's magnetic field. From the orbits of the satellites the density of the air layers through which they were passing was calculated, and found in some cases to be several times larger than the predicted values.

The third satellite was a veritable cosmic laboratory. It could measure the number and energy of micrometeorites hitting it, and carried a mass spectrometer. It measured its own electric charge, and the charges of the layers it passed through. It registered the atmospheric density and pressure, and carried a self-orientating magnetometer. It was also used for experiments on the control of orientation and internal temperature of the satellite vehicle.

Zodiacal Light, Meteorites and Earth Currents

An expedition to Egypt was organized to observe the zodiacal light and the polarization of the daytime sky, with specially developed instruments. These observations are being continued by the Helwan Observatory of the University of Cairo. The zodiacal light is also being studied at Aksenger, near Alma-Ata, in the U.S.S.R. (44° N., 76° E.), and by comparing these observations with those from Egypt it will be possible to find out how the properties of the zodiacal light depend on the ecliptical latitude.

In the U.S.S.R. eight stations have used radar to observe meteoric activity, and several formerly unrecorded streams of meteors were found, on January 15 and 16, 1958, for example, and on February 14 and March 9–15 of the same year. It was found that most sporadic meteors have elliptical orbits around the Sun, but some (less than 1 per cent of the whole) have been found which are definitely in hyperbolic orbits.

Earth-currents have been recorded continuously and pulsations of periods 1–4 sec. have been observed to occur simultaneously in the Arctic, Antarctic and middle latitudes. In the Antarctic large fluctuations occur in the amplitudes of the Earth potentials, up to about 1 volt/km.

Seismology

Seismic observatories were set up in the polar regions. There were six stations in the Arctic, and two in the Antarctic. These stations, in regions in which regular earthquake observations do not usually occur, give valuable information. The Antarctic stations observed about 600 earthquakes (in the two-year period beginning June 1, 1956), of which about 70 had epicentres south of 40° S.—however, no earthquakes have been detected which originated within the Antarctic mainland.

Microseisms were studied by many stations in the U.S.S.R. It was found that the microseisms observed in the European part of Russia originate mainly on the shores of Norway—no microseisms are observed when the storms are in the North Atlantic or on the shores of Greenland.

Okhotsk Sea—Pacific Ocean Structure

The crustal structure near the eastern coast of the U.S.S.R. was intensively studied. This region, extending to Kamchatka and the Kuril Islands, is of great interest. It has a high seismicity, with many shocks at all depths—this means that there is probably a deep major fault under the region. The deep seismic sounding method was used extensively; 3,300 km. of seismic profiles were taken at sea. The preliminary results show that the crust has different structures under the Okhotsk Sea, the Kuril Islands, and the oceanic plateau, with a thickening of the crust under the islands, and a substantial decrease of thickness under the oceanic plateau, where the crust is 12–18 km. thick (including the depth of the water). This region was covered also by aeromagnetic and sea gravitational surveys, and large anomalies were found (about 4,500 km. of sea gravitational surveys were taken).

The U.S.S.R. organizes the World Data Centre *B* for the International Geophysical Year: this has the task of collecting, keeping, and circulating data and results of all aspects of the work. Anyone wanting copies of such information should write either to Centre *B*1, Institute of Aeroclimatology, 33/35 Ulitsa Vorovskogo, Moscow; or Centre *B*2, Institute of Terrestrial Magnetism, 64 Chkalov Street, Moscow.

This article has been based on material supplied by Prof. V. V. Beloussov and V. A. Troitzkaya.

N. A. ROUTLEDGE

OBITUARIES

Prof. Wolfgang E. Pauli, For.Mem.R.S.

Unexpectedly to all but those near him at the time, Wolfgang Pauli died on December 15, 1958, at the early age of fifty-eight.

Born in Vienna, Pauli graduated in Munich, and worked successively at Göttingen, Copenhagen and Hamburg. Nowadays, however, his name is mainly associated with Zurich, where he was professor of theoretical physics at the Federal School of Technology for the past thirty years, broken only by five years in Princeton during the Second World War.

Though Pauli died so young, it is no exaggeration to say that he was one of the leaders of theoretical physics throughout the past forty years. At the age of nineteen he was commissioned by his teacher, Arnold Sommerfeld, to write the article on relativity for the "Enzyklopædie der Mathematischen Wissenschaften". At that time, general relativity was novel and its literature scattered and understood by few. The young Pauli succeeded in presenting the entire subject in a work which was immediately recognized as masterly and which, in its scholarly precision, remains unsurpassed to this day.

Having demonstrated so early the depth and clarity of his insight into physical theory, Pauli did not take long to prove that as an originator of new ideas he was equal to the greatest. In 1924 he enunciated his 'exclusion principle' in terms of which so much of the then existing knowledge of atomic structure fell into order : we owe to Pauli the introduction of the two-valued variable required to characterize completely the state of an electron, and when, in 1925, Goudsmit and Uhlenbeck took the important step of interpreting their variable as an intrinsic angular momentum, it was Pauli again who showed how this concept could be consistently incorporated into the scheme of quantum mechanics and how the exclusion principle could then be formulated definitively as a symmetry requirement satisfied by the wave function of an atomic system. This also became the basis of the powerful concept of the Fermi statistics governing the behaviour of electrons. In 1945 Pauli was awarded the Nobel Prize for Physics, primarily for these achievements.

Though the nineteen-twenties undoubtedly represented a peak in Pauli's creative work, he in fact never ceased to produce work of comparable depth and to exert a profound influence on the development of physics. He continued both to bring forth new ideas and to clarify and consolidate the ideas of others. It was Pauli who, in an informal letter, first threw out the suggestion that an unknown, uncharged and massless particle was emitted in every radioactive β-disintegration. This entity, to which Fermi gave the name 'neutrino', to-day has an assured and important place in our picture of Nature.

We can only name a few of Pauli's great contributions to theoretical physics. With Jordan and with Heisenberg he laid the foundations of the quantum theory of fields, a subject still very much the concern of pioneering theorists, and when after 1945 great advances were made in this domain, mostly by physicists of the younger generation, Pauli, almost alone among the founders of quantum theory, participated directly in these developments. Previously, in 1940, he had firmly laid one cornerstone of field theory, by giving a proof of the long-conjectured relation between the spin and the 'statistics' of any elementary particle. This result, so closely related to his great work of the 'twenties, gave Pauli himself particularly great satisfaction.

Pauli's writings are in daily use among research workers everywhere. Perhaps the work most greatly admired is his article on the principles of wave mechanics in the "Handbuch der Physik", Vol. 24, 1933. Younger theorists may perhaps not realize how much the orientation and emphasis of research to-day owe to the guidance given by Pauli in this and his many other writings.

Those whose good fortune it was to be close to Pauli at one period or another know how much more has been lost by Pauli's death than can be put into words. As a personality, no one more deserves to be described as unique. His rotund build and characteristic gait, his gestures and mannerisms, his sharp tongue and gleeful laugh will all be remembered vividly by his friends. Anecdotes around him abound, and the legend of the 'Pauli effect', spelling disaster to any apparatus he approached, is all but believed throughout the world.

When in personal contact with Pauli it was impossible to lose awareness of all his characteristics and of the sense of the extraordinary in his nature. As many of his students discovered, communication with him did not always come easily, least of all through formal lectures. But once one was drawn into discussion, the barrier was surmounted and the experience of sharing his thoughts became infinitely rewarding. Through his large correspondence he extended his influence far beyond his own Institute. With Pauli's death many a physicist has lost a guide and critic without equal.

Not all of us had the privilege of sharing his deeper thoughts on questions transcending his own science. In his later years particularly, his studies extended into the philosophical domain and a number of writings scattered at present but shortly to be published in a collected English edition testify to this.

All those who can look back to personal contact with Wolfgang Pauli feel a deep sense of loss. He will be remembered by all as a great scientist, an unforgettable personality and a sincere friend.

N. Kemmer

Prof. A. C. Pigou

During the first half of the twentieth century, the University of Cambridge had a galaxy of brilliant scholars, scientists and thinkers. Prof. Arthur Cecil Pigou was among the greatest of them, and by his death on March 7 the University, and in particular his College, King's, have suffered an irreparable loss.

Prof. Pigou will be remembered by economists so long as the development of their science is studied. The favourite pupil of the great Marshall, and chosen by Marshall to be his successor in the chair of political economy, Prof. Pigou built on the foundations which Marshall had laid. By his teaching, his books, his articles in economic and other journals, his membership of Royal Commissions, and his letters in *The Times*, he played a major part in winning for economists the wide authority which they have to-day.

His most important work, "The Economics of Welfare", went through many editions, and was translated into many languages; it became, indeed, like his "Study in Public Finance" and his "Theory of Unemployment", a standard text-book in most schools of political economy throughout the world.

His title, "The Economics of Welfare", illustrates admirably his basic approach to his subject. In his introduction to the first version of his short book on "The Political Economy of War", he described it further; speaking of the "extraordinarily complex system of exchange built round the motive of private money profit", which it was his life's task to analyse, he described the "grave flaws of this system; it involves great waste; it has meant for very many human beings weariness, discontent, hunger and pain". The economists' hope, he said, was "that by carrying out well and truly this task of positive analysis, this economic anatomy and physiology, they might help other men, better trained than themselves for the practical work of government and administration, to fashion remedies or palliatives for the many evils they descry". He would never 'talk shop', if he could possibly avoid it; but those who were fortunate enough to have him as their teacher soon learnt the warm but practical idealism by which he was inspired.

They learnt, too, the splendid simplicity of his character, and the complete, uncompromising integrity of his heart and mind. Some of them, especially those with whom he climbed the rocks of Cumberland, and the mountains of Switzerland, Austria and Norway, came to know his unique gift for friendship, and his courageous determination as a leader, whatever the difficulties with which he met. In 1925, when he was only forty-seven, he strained his heart by climbing two peaks in the Alps in one morning, before he was fully trained; in spite of this 'fibulation', a week later he completed a long, unknown and difficult climb, only to collapse when he had brought his party safely off the rocks; from that point he was transported to his hotel on mule-back; yet only a week after that he accomplished what was, perhaps, his most difficult lead up the face of the Aiguille de la Za, circumventing an iced-up chimney by a route that could only be classed as exceptionally severe. It was a great climb; but the 'fibulation' which he then defied ultimately undermined his health, and brought his mountaineering to an untimely end.

Pigou was extremely shy with strangers—unless they were under ten years old. But when a little boy of five accomplished a walk at Buttermere over Scarth Gap and the Haystacks, and back by the Miners' path, Pigou was so moved by admiration that he invited the five-year-old hero, *and* his parents, to tea in his lovely house, Lower Gatesgarth.

There are many of his Cambridge friends to whom King's, without him, will never seem the same. King's was, indeed, a perfect setting for a life of such blameless goodness, and of such eminent academic and practical achievement. Those who were at Cambridge before the First World War will remember the warmth and power of his eloquence in Union debates, and his vivid interest in philosophy and poetry. Everyone who knew him will remember how he despised and hated the senseless folly of war. The epilogue to the second version of his "Political Economy of War", written in 1939, has the passion and the moving eloquence of the Gettysburg oration: "We are at a start of a journey whose end we cannot foresee. Yet once again the young and gallant, our children and our friends, go down into the pit that others have digged for them. Yet once again men of greater age, we that, if it might be, would so gladly give for theirs our withered lives, we cumber the earth in vain. We wait and watch and—those who can—we pray. As an economist I have not the power, nor, as a man, the heart, to strain through a night so black to a dawn I shall not see".

Cambridge will see no more his erect and striking figure walking along the Backs; but it will be long before the memory of his noble spirit has passed away.

Philip Noel-Baker

NEWS and VIEWS

Imperial Chemical Industries, Ltd.: Sir Ewart Smith, F.R.S.

Sir Ewart Smith, who is retiring from the board of Imperial Chemical Industries, Ltd., obtained first-class honours in the Mechanical Science Tripos at Cambridge. He joined Synthetic Ammonia and Nitrates, Ltd. (later the Billingham Division of Imperial Chemical Industries, Ltd.), in 1923, and later played a part in the major development of the huge Billingham complex, becoming its chief engineer in 1932. He was seconded to the Ministry of Supply in 1942 to be chief engineer and superintendent of armament design. He returned to Imperial Chemical Industries, Ltd., in 1945, when he was appointed technical director, and was knighted for his war-time services in 1946.

Sir Ewart's responsibilities as technical director, and since 1955 as a deputy chairman of the Company, have not precluded his devoting a great deal of time and energy to other organizations. As a member of the British Productivity Council—he was its chairman in the early and difficult days following its formation—he has been nationally respected and admired by management and trade union leaders alike for his progressiveness, forthright honesty and vigorous leadership

Sir Ewart has also served on numerous other bodies, governmental and scientific, including the Advisory Council on Scientific Policy, the Committee on Scientific Manpower, the Northern Ireland Development Council, and as a vice-president of the Institution of Mechanical Engineers. He was elected a Fellow of the Royal Society in 1957 in recognition of his contribution to technology, and this year is president of Section G (Engineering) of the British Association. He is keenly interested in education, and is a governor of Christ's Hospital, his old school. Sir Ewart is to serve as chairman of the new council set up to assist the application of modern industrial techniques in the National Health Service.

National Science Foundation Antarctic Research Programme: A. P. Crary

Albert P. Crary has been appointed chief scientist of the newly established United States Antarctic research programme within the National Science

Foundation. Mr. Crary, a noted polar geophysicist, recently returned from two and a half years in Antarctica, where he was station scientific leader of the Little America Station and deputy chief scientist of the Antarctic programme of the U.S. National Committee for the International Geophysical Year. The United States Antarctic research programme has been established to co-ordinate the scientific efforts of Federal agencies with an interest in Antarctic research and to receive proposals by university scientists and independent investigators for polar research. The Foundation looks to the Committee on Polar Research of the National Academy of Sciences—National Research Council for recommendations regarding the desirability of proposed programmes. Mr. Crary will advise the Foundation in the planning of the scientific projects, selecting personnel and equipment, and will supervise the conduct of field investigations, data analysis, and publication. Mr. Thomas O. Jones is director of the Antarctic research programme of the National Science Foundation. Mr. Crary will maintain offices at the Foundation and at Cambridge, Mass., where he will continue his affiliation with the Geophysics Research Directorate, Air Force Cambridge Research Center.

Geography at Sheffield : Prof. C. A. Fisher

Mr. Charles Alfred Fisher, at present reader in geography in the University of Leicester, has been appointed to the chair of geography in the University of Sheffield in succession to Prof. D. L. Linton (see *Nature*, 182, 497; 1958). Mr. Fisher, who will take up his appointment in October, graduated at Cambridge with first-class honours in both parts of the Geographical Tripos. He was awarded a University Bartle Frere Research Exhibition in 1938 and for the next two years he undertook research at Cambridge. After nearly six years in the Army, Mr. Fisher took up an appointment in January 1946 as an assistant lecturer in geography at University College, Leicester, and later that year was appointed to a lectureship in geography at the University College of Wales, Aberystwyth, which he held until December 1949. Before returning to Leicester as a lecturer in 1951, Mr. Fisher held an appointment as senior research officer at the Institute of Colonial Studies, Oxford. In October 1958 the title of reader in geography in the University of Leicester was conferred on him.

In 1947 Mr. Fisher was awarded a Travelling Fellowship of the Royal Geographical Society which enabled him to make a series of study visits to Dutch universities and the Tropical Institute of Amsterdam in connexion with his researches on South-east Asia, and during the session 1953–54 he was a visiting lecturer in geography at Yale University, and was appointed Visiting Fellow of Trumbull College, Yale. Mr. Fisher has contributed chapters to several books and has published many articles on a wide range of geographical subjects, particularly on South-east Asia and the Far East.

Nuclear Technology at the Imperial College of Science and Technology, London

Courses of instruction and postgraduate research in the various branches of nuclear science and engineering given at the Imperial College of Science and Technology, London, include those on the theoretical and practical aspects of nuclear and high-energy physics (Physics and Mathematics Departments); a postgraduate course in nuclear power (Department of Mechanical Engineering); and a new course in nuclear technology (chemical) (Chemical Engineering Department). This one-year course, which commences in the session 1959–60, is under the supervision of Mr. G. R. Hall, reader in nuclear technology, assisted by Dr. H. D. Evans, Mr. S. Hartland and Dr. A. J. Swallow. In addition to topics relating to nuclear power production, such as fuel-element technology and the processing of irradiated fuels, a substantial part of the course will be devoted to the applications of radioisotopes as tracers and for non-destructive testing, and the possible uses of sources of radiation for inducing industrial-scale chemical reactions. Applications for admission should be made before June 1, on a form obtainable from the Registrar, Imperial College of Science and Technology, London, S.W.7.

Nuclear Training in the Biological Sciences in the United States

The United States Atomic Energy Commission has approved thirty-two new grants totalling 316,717 dollars to thirty-one American colleges and universities. These grants are part of a programme to assist colleges and universities to expand their facilities for training in radiation biology and in the use of radioisotopes in the fields of agriculture, veterinary medicine, medicine and pharmacy, public health and biology. The new grants bring to 1,810,707 dollars the total amount awarded in making 152 grants to 110 institutions since the Commission's programme was initiated in October 1957.

The Australian National University : Field Station for Astronomy

About a year ago the Department of Astronomy (Mount Stromlo Observatory of the Australian National University) initiated a survey to locate a suitable site for a field station. Excessive night cloudiness in Canberra and vicinity renders it impracticable to carry out at Mount Stromlo sustained long-range observational programmes. The intention is not to transfer major equipment from Mount Stromlo to the field station, but the University may want to place some future new equipment there rather than at Mount Stromlo. There is no question of transferring any of the research, teaching or administrative activities to the site of the field station. During the past year, tests for night cloudiness have been carried out at four localities, all of which are hill tops rising 700–1,000 ft. above the level of the surrounding plain, three in New South Wales and one in Victoria. According to the records gathered to date, Natimuk (Victoria) has the largest percentage of clear nights (65 per cent over 122 nights), Griffith has 54 per cent over 266 nights, Condobolin 47 per cent over 263 nights. Mount Stromlo had only 28 per cent clear over the same interval. Alectown and Lake Cargellico both show 40 per cent clear. All observations refer to the first half of the night.

Astronomical tests are to be initiated at various sites, notably near Natimuk, Griffith and Condobolin. Provided arrangements can be made for temporary occupation of the site, access roads, electricity supply and telephone service, a control station will be set up near Griffith and one of the smaller telescopes from Mount Stromlo Observatory will be moved there, with the intention of operating it for a period of eighteen months. Mobile telescopic equipment will be set up at the other sites under consideration, and each site will probably be occupied several times for periods of about two weeks at any one time.

Russian *Journal of Inorganic Chemistry*

STARTING with the January 1959 issue, the Chemical Society is to publish, with the support of the Department of Scientific and Industrial Research, a cover-to-cover translation of the monthly journal, *Zhurnal neorganicheskoi Khimii*, a publication of the Academy of Sciences of the U.S.S.R. The translation will be undertaken for the Society by Infosearch, Ltd., and the Society has appointed Prof. P. L. Robinson as executive editor. He will be assisted by an advisory panel of distinguished inorganic chemists. The sale and distribution of the journal will be undertaken by Cleaver-Hume Press, Ltd., 31 Wright's Lane, London, W.8, from whom a detailed prospectus giving the scope of this journal may be obtained. Translations will be issued in monthly parts as soon as possible after the Russian original is available. The subscription rate will be £30 (United States, 90 dollars) per annum, but universities and technical colleges may subscribe at a discount of 25 per cent. Single issues can be purchased at £4 (12 dollars) per copy. The Society also hopes to start the publication within the next year of translations of the Russian *Journal of Physical Chemistry* (*Zhurnal fizicheskoi Khimii*) and *Progress in Chemistry* (*Uspekhi Khimii*).

School Mathematics

USEFUL comments on the teaching of mathematics in schools are to be found in the Spring 1959 issue of *Forum* (**1**, No. 2). The headmaster of a junior school, the head of the mathematics department at a comprehensive school and a university professor of mathematics all agree that the aversion to mathematics which is found in so many intelligent adults was implanted in the primary school. According to one observer, mathematics in the primary school consists entirely of computation. "Available text-books present dreary, intelligible masses of sums instead of challenging children to think, to reflect on how, when and where, with numbers and space relationships." Instead of imparting an appreciation of number relationships in the way advocated by Piaget, most mathematics teaching in primary schools consists of a series of tricks which have little connexion with the life of the child. Suggestions for making the teaching more related to the child's experience are described in two of the articles, while Prof. R. L. Goodstein, of the University of Leicester, also advocates research to find a more enlivening syllabus and more successful methods of presentation.

Control of Exhaust Fumes

IN reply to a question in the House of Commons on March 24 regarding research into the control of the emission of diesel oil and petrol exhaust fumes from vehicles, Mr. H. Nicholls said that the results of work on combustion in diesel and petrol engines, carried out by the Motor Industry Research Association and the British Internal Combustion Engine Research Association and elsewhere, showed that the greater part of the smoke from such engines could be prevented by proper adjustment, running and maintenance. The Warren Spring Laboratory of the Department of Scientific and Industrial Research had tested a catalytic device which effectively reduced the pollution from petrol engine fumes. Mr. Nicholls agreed that unpleasant fumes were often due to absence of proper maintenance.

National Research Development Corporation of India

THE fourth annual report of the National Research Development Corporation of India, which includes the statement of accounts for the period ending March 31, 1958 (pp. 20. New Delhi: National Research Development Corporation of India, 1958), records 59 inventions reported for development by eighteen research institutions and individuals, making a total of 447. Five new patent applications were filed and seventeen new licence agreements were negotiated. New projects for refining cotton seed oil, for white cement from feldspar, and for a fluidized-bed technique for textile processing were instituted, and a project for pine oil from Indian turpentine was completed. Progress is reported in those for production of phthalic anhydride by fluidized-bed oxidation of coal tar oils, for copper chlorophyll, for bamboo mechanical pulp, the de-ionization of sugar cane juice and for a thermoelectric generator.

The Civic Trust

FOUNDED just over a year ago to ensure that community developments are made with good taste and dignity and to give delight to all inhabitants, the Civic Trust has already acquired a momentum which should lead to a future of promise and fulfilment. In collaboration with the B.B.C. Television Service, four useful films have been produced showing how the Trust is waging war on ugliness. The threatened demolition of part of the Close of Dunblane Cathedral has been averted by prompt intervention by the Trust. As the first of a series of 'live' experiments, Magdalen Street, Norwich, is being redecorated in accordance with an over-all scheme prepared by the Trust. The Trust is also to develop a system of amenity awards, the objects of which are to encourage good local architecture and building of all kinds which can be said to make a desirable contribution to the civic and rural scene as a whole, and to stimulate interest in all other types of physical development. Details of the awards can be obtained from the Civic Trust, 79 Buckingham Palace Road, London, S.W.1.

South Australian Museum

THE most recent issue of the *Records of the South Australian Museum* (13, No. 2; 1958) forms another sumptuous part of the current volume, with 156 pages of text and twenty-four excellent plates. Most of the papers are by members of the staff of the South Australian Museum and include contributions on the aboriginal cave paintings at Sleisbeck, a revision of the ghost moths, new cretaceous fossils from New Guinea, Australian beetle-mimicking bugs of the family Lygaeidae, and on the Potoroinea (a group of central Australian mammals). Such a publication gives evidence of a progressive museum with a staff undertaking research of a high order.

Aviation Psychology

THE military Air Forces and civilian air lines of every country are aware of the many psychological factors involved in safe flying, and of the difficulties in selecting and training suitable air-crew. But only in the United States and, to a lesser extent, in Britain are there sufficient psychologists employed in the field of aviation to develop a systematic attack on these problems. Thus in an attempt to co-ordinate and further their activities, the aviation psychologists of Western European countries have formed an association; and a recent monograph (Aviation

Psychology in Western-Europe and a Report on Studies of Pilot Proficiency Measurement. Publication No. 1 of the Western-European Association for Aviation Psychology. Pp. 64. Amsterdam: Swets and Zeutlinger, 1958. 15*s*.) contains a series of reports on the present position of their work from representatives of most of the countries concerned; the absence of British civilian air-line representatives is conspicuous. It is interesting to learn that most Air Forces or companies are achieving better selection of pilots by scientific testing (despite considerable variations in the relative emphasis placed on paper-and-pencil tests, apparatus tests and clinical assessments). But it is disappointing to find so little attention, outside the British Institute of Aviation Medicine, to 'human engineering' and training problems such as the effects of stress and fatigue on air-crew, and the design of aircraft equipment and simulators (synthetic training devices). Much the most stimulating paper is one contributed by the American psychologist, Dr. C. W. Bray, on the detailed recording of pilot performance.

Statistical Review of England and Wales for 1956

The Registrar General has recently issued the Commentary Volume on the Statistical Review of England and Wales for 1956 (pp. xvi+294. London: H.M. Stationery Office, 1958. 16*s*. 6*d*. net). As has become established practice, this volume includes some special analyses, as well as commentary on the vital events of the year to which it relates. There is included a nuptiality table for 1951–55, which has been computed in connexion with the fertility analysis of the 1951 census. Such a table is similar to a life-table, but shows the survivors at various ages up to fifty by marital status. The very high rates of marriage prevailing in 1951–55 are indicated by the fact that of 100,000 females, 90,656 survive to age fifty, of whom only 4,837 have never been married. Of the group of males surviving at age fifteen, only half are still single at twenty-five; in the case of females the corresponding age is twenty-two. Another special feature included is a comparison of causes of death as ascertained after autopsy with those given on death certificates. The comparison applies to deaths occurring in a number of selected hospitals, and deaths certified by general practitioners are not included. It is shown that in 19 per cent of all cases, new facts were ascertained by the pathologist which had not been reported by the clinician. It was also apparent that deaths from cancer of the lung were under-recorded, in spite of the greater diagnostic facilities that were available.

Insect Toxicologists' Information Service

At a meeting held during the tenth International Congress of Entomology at Montreal, insect toxicologists agreed to co-operate with Dr. D. Dresden of the University of Utrecht in establishing an Insect Toxicologists' Information Service. The first Bulletin of the information service was issued recently (Insect Toxicologists' Information Service, Bulletin No. 1. Pp. 106. Vondellaan 6, Utrecht, 1958) by Dr. Dresden. The object of the Service is to enable insect toxicologists all over the world to keep in touch with one another and to be kept up to date with each other's research activities. The Bulletin, which is to be issued annually, is designed for this purpose. The names of the workers on insect toxicology are given, with the laboratory in which they work and some indication of their interests. Some account is also given of the biological material that they work with, since interchange of material may facilitate research. The main body of the Bulletin consists of short notes from the workers themselves on the work they are doing, and it is necessary to submit these notes in order to receive a copy of the Bulletin. Providing the insect toxicologists fulfil their promise to co-operate with Dr. Dresden by submitting their notes regularly, this service should greatly benefit research in this field.

The Nessim Habif Prize

The University of Geneva will award in 1959 the Nessim Habif Prize of 10,000 Swiss francs to an author of a work or to an inventor who has made an important contribution to the knowledge or uses of plant cellulose or its synthetic derivatives. Manuscripts must be submitted by May 1 to the Doyen de la Faculté des Sciences de l'Université de Genève, Université, rue de Candolle, Genève, from whom further information can be obtained.

Harkness Fellowships of the Commonwealth Fund

The British Committee of Award of the Commonwealth Fund has announced the following elections, among others, to Harkness Fellowships for 1959, tenable for one or two years in the United States: R. H. Cassen (London School of Economics), economics; C. B. Cox (King's College, London), palæontology; R. N. Curnow (Aberdeen), biostatistics; V. J. Emery (Clare College, Cambridge), nuclear physics; C. W. J. Granger (Nottingham), economics; J. F. Hodgess Roper (Magdalen College, Oxford), international economics; S. C. Hunter (Armament Research and Development Establishment), theoretical mechanics; J. L. Jinks (Birmingham), genetics; A. D. McLachlan (Trinity College, Cambridge), theoretical chemistry; G. P. McNicol (Glasgow), medicine; W. T. Norris (Pembroke College, Cambridge), engineering; M. L. V. Pitteway (Queens' College, Cambridge), radio physics; D. C. Smith (Queen's College, Oxford), botany; J. B. Taylor (Atomic Weapons Research Establishment), theoretical physics.

International Oceanographic Congress

The American Association for the Advancement of Science is to hold an International Oceanographic Congress at the United Nations Building in New York, during August 31–September 12. The Congress is being planned in co-operation with the International Advisory Committee on Marine Sciences of Unesco and the Special Committee on Oceanic Research of the International Council of Scientific Unions. The Congress has the endorsement of the International Association of Physical Oceanography of the International Union of Geodesy and Geophysics. The programme has been designed to afford discussion among scientists interested in diverse fields of specialization within oceanography. Governments as well as universities and scientific organizations abroad are sending delegates to the Congress. It is also suggested that research vessels be sent to New York for the duration of the Congress, to make it possible to exhibit instruments used at sea and to display the most recent data and collections of biological and geological samples and chemical techniques. Further information can be obtained from the American Association for the Advancement of Science, 1515 Massachusetts Avenue, N.W., Washington 5, D.C.

Announcements

Prof. A. R. J. P. Ubbelohde, professor of thermodynamics at the Imperial College of Science and Technology, London, has been appointed director of the Salters' Institute of Industrial Chemistry on the retirement of Sir Alfred Egerton on June 30.

Allan Ray Putnam has been appointed managing director of the American Society for Metals, a new position established by the Board of Trustees following the death last May of William H. Eisenman, who was national secretary and executive head of the Society for forty years.

Mrs. Elwyn Davies, of Llandaff, Cardiff, who is a member of the Archæology and Art Committees of the National Museum of Wales and of the Board of Celtic Studies of the University of Wales, and Mr. John C. P. de Winton, of Brecon, have been appointed members of the National Parks Commission. Mrs. Davies will fill the vacancy left by the late Lady Hopkin Morris, and Mr. de Winton, who is a member of the Breconshire Education Authority, has been appointed as another representative of Welsh interests.

The following were recently elected as officers and members of Committee of the Society for the Bibliography of Natural History: *President*, Dr. J. Ramsbottom; *Hon. Secretary and Treasurer*, A. C. Townsend; *Committee*, G. F. Elliott, Dr. F. C. Fraser, F. J. Griffin, W. T. Stearn, C. K. Swann, Dr. D. W. Tucker.

The annual general meeting of the Antiquarian Horological Society will be held at the Science Museum, South Kensington, on May 1. The new honorary secretary of the Society is Mr. J. C. Stevens, 53 Woodfield Crescent, Ealing, W.5, from whom further information can be obtained.

A meeting will be held to consider a proposal that an International Congress on Corrosion be held in London in 1961 under the sponsorship of the Society of Chemical Industry. The meeting will be held at 14 Belgrave Square, London, S.W.1, at 3 p.m. on April 20, and all persons interested in the proposal are invited to attend.

The fifteenth Annual National Electronics Conference will be held at the Hotel Sherman, Chicago, during October 12–14. Abstracts, no longer than two hundred words, must be received by Mr. E. Van Valkenburg, Electrical Engineering Department, University of Illinois, Urbana, by May 1.

The second international conference on Medical Electronics will be held in the Unesco Building, Paris, during June 24–27. Further information can be obtained from Dr. C. N. Smyth, University College Hospital, Gower Street, London, W.C.1.

The twelfth Brookhaven Symposium in Biology, on Structure and Function of Genetic Elements, will be held during June 1–3. Sessions will be held on: structural aspects of nucleic acids; biochemical activities of nucleic acids; the gene; structure and duplication of chromosomes; nuclear–cytoplasmic relationships. Further information can be obtained from Dr. M. Levine, Brookhaven National Laboratory, Upton, New York.

The second symposium on X-ray Microscopy and X-ray Microanalysis will be held in Stockholm during June 15–17. The symposium will deal with new developments in X-ray microscopy and X-ray microanalysis as well as applications of these techniques. Further information can be obtained from Dr. G. Höglund, Institutionen för Medicinsk Fysik, Karolinska Institutet, Stockholm 60, Sweden.

The Italian National Committee for Nuclear Research is organizing a Congress on Nuclear Energy to be held in Rome during June 16–20, during the Sixth International Exhibition on Electronics and Atomic Energy. Further information can be obtained from the secretary of the Congress, Mr. Roberto Levi, Comitato Nazionale per le Ricerche Nucleari, Via Belisario 15, Rome.

The Advisory Group for Aeronautical Research and Development of Nato is holding a meeting on "Chemistry of Propellants" in the Nato Headquarters Building, Palais de Chaillot, Paris, during June 8–12. During the first four days the following themes will be developed: (1) properties and preparation of propellants; (2) theoretical and experimental performance evaluation; (3) fundamental studies; (4) sources, availability, and estimated costs of propellants. The fifth day will be devoted to a round-table discussion on "Basic Problems in Propulsion".

The European Conference for Industrial Management on "Industrial Prospects in Nuclear Energy", organized by the European Nuclear Energy Agency, will be held at the Palais des Congrès, Stresa, during May 11–14. There will be eight sessions, devoted respectively to a survey of European nuclear energy programmes; the economics of nuclear power; financing such programmes; legal problems involved; management problems; the market for materials; the market for equipment; and the market for instruments. Further information can be obtained from the Information Officer, European Nuclear Energy Agency, Organization for European Economic Co-operation, 38 Boulevard Suchet, Paris 16^{e}.

The Development Commissioners, in association with the Ministry of Agriculture, Fisheries and Food and the Scottish Home Department, are prepared to award postgraduate training grants in fishery research tenable from October 1, 1959. These grants are intended to enable selected candidates to undergo a specified course of training to fit them for the investigation of problems in marine or freshwater science. Candidates must be nominated by a senior member of a university department. Provisional applications will be accepted from candidates who have not yet sat their final examination or who have not yet been informed of the result. Further details and forms of application, returnable by May 20, can be obtained from the Secretary, Development Commission, 3 Dean's Yard, Westminster, London, S.W.1.

Cornell University annual summer Laboratory Course in Techniques and Applications of the Electron Microscope is to be held during June 15–July 3. The course is planned to meet the needs of senior research workers in the field of electron microscopy. Registrations will be limited in number, to provide ample facilities for the members to pursue extensive laboratory work in their special fields, at introductory or advanced levels depending on their previous experience. The course of lectures is designed to give members an intensive survey of basic theory, as well as interpretation of results and application to research problems. Further information and forms of application can be obtained from Prof. B. M. Siegel, Rockefeller Hall, Cornell University, Ithaca, New York.

HYPERSONIC FLOW

ON December 15, some two hundred representatives of the research establishments, the aircraft industry and the universities attended an all-day discussion on hypersonic flow sponsored by the Royal Aeronautical Society and held, under the chairmanship of Dr. G. W. H. Gardner (Royal Aircraft Establishment, Farnborough), in the rooms of the Institution of Mechanical Engineers.

An introductory paper surveying the problems of hypersonic aerodynamics was read by Mr. R. J. Monaghan (Royal Aircraft Establishment, Farnborough). The term 'hypersonic' can generally be applied to flight at Mach numbers greater than about 5, for it is at speeds of this order that the linearized equations of supersonic flow become inadequate, boundary layers of increased thicknesses begin to interact appreciably with flow fields around slender bodies and aerodynamic heating assumes major importance. A further boundary occurs at Mach numbers of the order of 8–9, when there is sufficient kinetic energy to provide some dissociation of the oxygen molecules in air, and the amount of dissociation increases with increasing Mach number above this value.

In designing for the alleviation of aerodynamic heating there are two distinct cases. The first relates to the uncontrolled re-entry of a freely falling body, for which a high-pressure drag shape is required; the second refers to sustained flight, for which a shape with low-pressure drag is probably better, radiation giving appreciable control of surface temperature. Low-pressure drag accords with design for aerodynamic efficiency and there is scope for research on three-dimensional lifting shapes.

The strong curved bow wave moving ahead of the body which is a characteristic of hypersonic speed implies that no real distinction can be drawn between blunt and sharp noses; moreover, the necessity for avoiding excessive rates of heat transfer means that the nose must be blunted. Some distinction can be made, however, between bodies in which the curvature varies slowly along the surface, and flat-faced bodies in which a distinct shoulder occurs.

In his paper on general characteristics of hypersonic flow fields, Dr. R. N. Cox (Armaments Research and Development Establishment, Fort Halstead) gave a historical survey of early work on hypersonic flow and discussed the problems of predicting pressure distributions over blunt-nosed slender bodies.

Expressions have been obtained by many authors for predicting these pressure distributions, but unfortunately the estimates do not agree with experimental measurements. It has now become generally accepted that the magnitude of viscous interaction is a function of Reynolds number based on the thickness of the leading edge; above a certain value of this Reynolds number (that is to say, if the leading edge is blunt) the pressures induced near the leading edge of a body are almost entirely due to inviscid flow effects. Afterwards, there had been much theoretical work on the details of inviscid flow fields, and some promising approximate methods have appeared—for example, the use of Newtonian flow followed by a Prandtl–Meyer expansion for flow over round noses, and the application of the intense blast-wave analogy for predicting induced pressures over the rear portion of the body.

Problems of truly blunt bodies were considered by Dr. K. W. Mangler (Royal Aircraft Establishment, Farnborough) in his paper on special aspects of hypersonic flow fields. Following the bow wave ahead of a blunt body is a region of subsonic flow, and very reasonable estimates of the flow variables in this region can be obtained from inviscid theory, provided that allowance is made for the variation of entropy across the shock, and that the equation of state is adjusted to make allowance for the different degrees of freedom excited in the molecules of the gas. Accordingly, consideration was given to a theoretical model of an inviscid flow at very large Mach number and with a ratio of enthalpy to internal energy approaching unity. Attempts to extend this work to cover the more general case of arbitrary large Mach numbers and more realistic values of the enthalpy – internal energy ratio have shown the necessity for adopting numerical techniques.

Many of these techniques deal with the inverse problem of finding the body to fit a given shock shape, which simplifies the procedure considerably, and on these lines a marching technique can be devised. The non-viscous concept gives satisfactory results for the forward-facing surface, but, behind the shoulder of the body, viscosity has to be taken into account, and it is necessary to match the values of the flow properties at the outer edge of the boundary layer with those of the flow entering from the inviscid region.

A paper on hypersonic boundary layers with special reference to aerodynamic heating by Dr. L. F. Crabtree (Royal Aircraft Establishment, Farnborough) emphasized the importance of the leading edge in problems of heat transfer. The rate of heat transfer to a bluff body, including dissociation effects, can be investigated analytically.

The dense layer of air near a highly cooled surface is relatively unaffected by pressure gradients along the surface, a concept which proved very useful in calculations of turbulent boundary layers for blunt bodies; if true local conditions are used, the intermediate enthalpy method is very useful, for undissociated flow, for both laminar and turbulent boundary layers at Mach numbers up to 10.

Dr. K. W. Mangler had mentioned the problems of lifting bodies with their associated problems of vortex and bubble type separations. From the point of view of low drag the former would appear preferable, but a planned use of the latter also has possibilities; for example, a spike protruding from the nose of a blunt body can reduce the drag. However, difficulties arise in this case, since experiments have shown high heating-rates when the flow becomes re-attached; indeed, the overall heat transfer might be higher than on the basic bluff body without a spike. Other methods have been suggested for the reduction of aerodynamic heating-rates, including ablating surfaces and transpiration cooling; for the latter method, experiment has shown that quite modest amounts of coolant blown through a wall can produce a considerable reduction in the heating-rates.

Methods of studying experimentally some of the problems of hypersonic flows were surveyed by Dr. D. W. Holder (National Physical Laboratory, Teddington). Some of the new problems can be studied with techniques which do not differ in principle from those used in research at supersonic speeds. However, to simulate fully the very high temperatures of hypersonic flight it is usually necessary to employ heaters or tunnels of unconventional design, frequently having a very short running time, or to make tests with a model launched or propelled at a very high velocity. In such tunnels the working gas is usually heated by compression, in a shock tube or by a system of shock waves, or by the discharge of electrical energy.

In addition to the usual wind-tunnel measurements of aerodynamic loading and heat transfer, the pressure, temperature and density of the working gas are required ; the degrees of dissociation and ionization and their variation with temperature and time are other properties which have to be measured within the brief period of steady flow provided by the test facility.

Types of facility at present in use include helium tunnels, arc-heated and plasma jets, hypersonic gun-tunnels, shock tubes, shock tunnels, 'hot-shot' arc-driven tunnels, free-flight wind-tunnels and free-flight rocket-propelled models ; none of these is able to simulate fully all the required conditions, but each is able to assist in investigation of the problems of some part of the hypersonic regime.

Prof. M. J. Lighthill (University of Manchester) began his paper by a detailed study of the dynamics of dissociating oxygen. Two mechanisms of dissociation exist, one by collision with another particle, the other by absorption of a photon of light. The wave-lengths of light required are in the ultra-violet range (especially 1300–1750 A.), and although at high altitudes the wave-lengths are present in sunlight, they are almost entirely absorbed by the dissociation mechanism. There is practically no light of this wave-length present at altitudes less than 60 km., and at lower altitudes all dissociation is due to collisions.

Conversely, recombination can be effected in two ways : three-body recombination and two-body combination with emission of light. The latter predominates at very low densities, say, less than 10^{-8} gm./cm.^{3}. Where aerodynamic forces are important, three-body recombination is more likely to occur.

The energy required to dissociate an oxygen molecule can be described as the kinetic energy that it would have if its speed were 5·5 km./sec. Thus, some dissociation will occur around any body travelling through oxygen at this speed. Not all molecules will be dissociated, for some of the energy will go to increase the translational, vibrational and rotational energy of the molecules.

On passing through the shock wave ahead of the body, the kinetic energy of the molecule is converted almost entirely to translational and rotational energy, and a transitional region exists before dissociational equilibrium is reached ; however, equilibrium is reached so rapidly that no direct measurements of satisfactory accuracy have been made in this region.

During dissociation the pressure increases, and this has the effect of compressing the air cap between the shock wave and the body. At very low densities the thickness of the boundary layer is comparable with that of the compressed air cap, and it has been concluded that if the surface were cooled to a temperature not much greater than that of the free stream, then the cooled boundary layer would have an effective negative displacement thickness.

A paper by Dr. J. A. Shercliff (University of Cambridge) on possible aeronautical applications of magnetogasdynamics began by stating that, in the equilibrium state, the ionization process is amenable to the same thermodynamic and statistical-mechanical treatment as the dissociation process. However, it is possible in hypersonic flow that ionization, like dissociation, can fail to reach equilibrium, and the ionization relaxation process behind a bow shock wave can occupy a region comparable in extent with the dimensions of the vehicle.

Magnetogasdynamics is generally understood to exclude the type of electron behaviour which belongs to plasma physics, and the thermodynamics of the gas is considered to be unaffected by the magnetic field.

The interaction of velocity fields with magnetic fields produces the novel features of magnetogasdynamics, and many parallels with fluid dynamics exist—for example, the so-called magnetic Reynolds number measuring the relative power of the convective and diffusive processes. If this is large, a magnetic boundary layer occurs (the skin effect, well known to electrical engineers), but in aeronautics, magnetic disturbances diffuse much more rapidly than viscous disturbances, and the viscous boundary layer can be ignored when studying the field distortion.

In aeronautics the most obvious application of magnetogasdynamics lies in its use to modify forces on, or heat transfer to, a vehicle. Drag can be produced in midstream away from the surface of a body, heat transfer to stagnation points and skin friction can be reduced by suitably orientated magnetic fields, and transition or separation of the boundary layer can be controlled. An interesting application is that in which an electrical field supplies energy through electrodes to air, accelerating it for propulsive purposes, or the converse case in which air in motion is used to generate electrical energy, which is then supplied to the vehicle to drive auxiliary systems.

The weight penalty will probably confine the use of electromagnetic rockets to interplanetary space vehicles assembled in satellite orbits. Land-based experimental facilities are not affected by the weight penalty and the possibility of high-enthalpy test plant seems attractive. Another possible use lies in the reduction of heat transfer to hypersonic nozzles.

The final paper, on aerodynamic problems of manned space vehicles, was given by Mr. T. R. F. Nonweiler (The Queen's University of Belfast). Any analysis of a project designed to carry a man into orbit and return him safely to Earth must consider the need to limit the accelerations and retardations of his passage and the temperature of his environment. There is no need to fear excessive accelerations in a powered ascent ; even with existing fuels a two-stage rocket would not necessarily involve accelerations of more than 10 g.

Descent from an orbit could be effected by the use of a glider vehicle employing aerodynamic lift ; an alternative is the so-called 'parachute re-entry' using aerodynamic drag, although whether or not a 'parachute' is employed is immaterial, for if the shape and drag of the vehicle remain constant the deceleration always has the same characteristic variation in time, reaching a maximum value of about 8*g*. Deceleration and aerodynamic heating, except in the region of the leading edge, are much reduced by employing lift in the descent, although the provision of lifting surfaces entails an increase in weight of the vehicle and the unusual stability and control characteristics pose interesting problems.

The most critical conditions will probably be encountered not in the return from a successfully accomplished orbit, but in emergency re-entry from an abortive ascent. In meeting this contingency there appears to be some advantage in the glider type of vehicle rather than the zero-lift type, but the evidence is by no means conclusive at present.

The question of a successful landing involves many possibilities. An airfield would be a remarkably elusive target in an unpowered glide which, as a result of emergency or mistake, might be initiated over the Pacific Ocean. Probably the glider would have to be regarded as expendable, the occupant being ejected by capsule at a low altitude.

B. E. BEADLE

INTERFACIAL PHENOMENA

THE biennial conference of the Physical Society, on solid state physics, was held during December 18–20 at the Cavendish Laboratory, Cambridge, under the general title of "Interfacial Phenomena". The conference was attended by about two hundred delegates and twenty-eight papers were presented, which fell into three major groups describing, respectively, various effects associated with films deposited in vacuum, the nature of solid – liquid interfaces and the formation of electrodeposited films, and the structure and properties of internal surfaces. The conference brought together physicists, physical chemists and metallurgists, each with a different approach to the study of interfacial phenomena.

In introducing the papers on films deposited in vacuum, D. W. Pashley (Tube Investments Laboratory, Hinxton Hall) gave first a brief historical survey of the experimental work on the growth of oriented deposits on substrates. He defined the terms 'epitaxy' and 'misfit' and showed that under some conditions epitaxy only occurred with a misfit of less than 15 per cent, but that in many cases misfits of much larger than 15 per cent could be tolerated. The limitations of the various techniques used for the investigation of epitaxy were then outlined, the great power of the electron microscope being emphasized.

The potentialities of the electron microscope in this field of study were fully exploited by G. A. Bassett (Tube Investments, Hinxton Hall). His experiments on nucleation, orientation and growth of vacuum-deposited metal films on ionic and metallic substrates showed that an oriented layer of gold of about 10 A. mean thickness, deposited on a single-crystal silver substrate, formed nuclei of 20–200 A. diameter which grew in size rather than number until a continuous film was formed at a mean deposit thickness of about 50 A. When gold was deposited on rock salt a similar effect was observed, but there the gold nuclei formed preferentially at slip and cleavage steps on the rock salt surface.

Reflexion electron diffraction techniques were used by R. C. Newman (Associated Electrical Industries, Aldermaston), A. Glossop and D. W. Pashley (Tube Investments, Hinxton Hall), to study the deposition of copper on silver maintained at different temperatures. They found diffraction patterns characteristic of copper with its normal lattice constant when the mean film thickness was 0·8 A. and the substrate temperature 20° C., but by increasing this temperature to 300° C. copper patterns were obtained at a mean film thickness of 0·2 A. These results showed that at above a critical mean thickness of much less than one atomic layer, aggregation of the copper occurred on the substrate surface rather than the formation of a uniform film.

Somewhat different results on the influence of imperfections in the substrate upon the mode of epitaxial growth were presented by W. J. Dunning and P. G. Fox (University of Bristol). They examined, with the optical microscope, the growth of ammonium iodide upon mica and observed a uniform epitaxial film spreading outwards until cleavage steps on the mica were reached and then a pyramidal form of growth of the iodide crystals was initiated. The importance of the substrate orientation upon kinetics of film growth was demonstrated clearly by the experiments of J. D. Lawless (University of Virginia), who had oxidized spherical single-crystals of copper in air and in copper sulphate solutions. Differences in the thickness of oxide film were shown by changes in the interference colours from different regions of the spherical surface. Examination by electron diffraction and electron microscopy showed differences in the preferred orientation of the polycrystalline oxide film on various zones of the single crystal.

The epitaxial growth of ice crystals on various substrates and its possible effect upon the formation of rain were discussed by B. J. Mason (Imperial College of Science and Technology, London). He described observations on the nucleation of ice on covellite which showed that after nucleation ice crystals may spread laterally on the surface without thickening. The experimental technique involved observing, with the optical microscope, the interference colours produced by the thin crystals on the cleaved covellite surface, and Dr. Mason illustrated his results with colour micrographs of kaleidoscopic variety.

Two further papers on electron diffraction studies of epitaxial growth were presented by M. Blackman (Imperial College of Science and Technology, London), who discussed the epitaxial polymorphism of thallium and cæsium halides, and H. Wilman (Imperial College), who gave some new examples of epitaxy. He showed many diffraction photographs illustrating the different forms of epitaxial growth on ionic, organic and metallic substrates of deposits condensed *in vacuo* or formed by chemical action.

A group of papers on the properties of surface films were presented next. J. A. Bennet (British Scientific Instrument Research Association) described an apparatus which enabled him to measure the electrical resistivity of a gold film as it was being deposited on either alumina or on a substrate of bismuth oxide on alumina. He found the resistivity decreased as the thickness of the film increased, an effect which he attributed to changes in continuity of the film. This conclusion was in agreement with the results given by previous speakers, who showed that in the earliest stages of deposition an epitaxial film was not continuous.

The adhesion of evaporated metal films to glass was discussed by C. Weaver and P. Benjamin (Royal Technical College, Glasgow). The load required to leave a clear scratch through a metal coating deposited in vacuum on a glass substrate was measured and found to depend upon the time which had elapsed after deposition in the case of iron and aluminium, but not for gold. The adhesion of the gold could be attributed to Van der Waals forces, but the rapid increase in the adhesion and its greater value in the case of iron and aluminium could only be accounted for if some chemical bonding occurred between the glass and evaporated layer. Further experiments which tended to confirm that oxygen was necessary to produce this bonding were then described. An entirely different approach to the problems associated with deformation of evaporated layers on substrates was adopted by T. Evans (Tube Investments, Hinxton Hall). An oriented film of gold about 300 A. thick was evaporated on to a single crystal of silver, and on top of the gold film a polycrystalline film of carbon, platinum, iron or chromium was deposited. The composite specimen was then deformed. By dissolving away the silver a specimen thin enough to be examined directly by transmission in the electron microscope remained. This revealed that the presence of the polycrystalline layer modified the slip distribution in the substrate. Dr. Evans concluded that some of the effects could be attributed to adhesion between the polycrystalline and the gold layers.

The first section of the conference was completed by two papers on the surface tension of metallic interfaces. H. Mykura (University of Glasgow) showed that the shape of the grooves produced at grain boundaries when a metal surface is etched thermally depended upon the difference of orientation between the grains, while J. M. Blakely and H. Mykura (University of Glasgow) calculated how an exposed metal surface having a sinusoidal form would change its shape on heating by a process of self-diffusion leading to mass transport against curvature gradients.

Five papers were presented describing phenomena associated with solid – liquid interfaces. Prof. F. C. Frank (University of Bristol) discussed the kinematics of deposition and dissolution profiles of crystals and showed how the theory of kinematic waves was applicable to this study, while a review of phenomena at metal – electrolyte interfaces was given by R Parsons (University of Bristol), who summarized current ideas about the structure of the electrical double layer between a metal and an electrolyte.

The work of the J. Lucas research group on electrodeposition was introduced by M. J. Pick (University of Birmingham). After reviewing earlier work on electrodeposition he described their new investigations on the deposition of copper on single crystals and polycrystalline cube-texture copper. As in the case of vacuum deposition, the electro-deposited metal initially formed nuclei which eventually grew into each other, forming well-defined crystals. The shape of the nuclei was found to vary with the orientation of the substrate. Further aspects of the work of this research group were then presented by G. C. Storey, T. B. Vaughan and V. R. Howes (University of Birmingham). Changes in surface topography with changes in cathode orientation were determined by detailed light and electron optical examination, and the results obtained were explained in terms of bunching of the growth layers in the manner described in the earlier paper by Prof. Frank. A ciné film of deposits growing in a cell on the stage of an optical microscope were shown ; in one sequence growth by a spiral mechanism was clearly recorded.

Further experiments on the growth of electrodeposits of face-centred and body-centred cubic metals on single crystals of face-centred cubic substrates were described by H. Wilman and A. R. N. Reddy (Imperial College of Science and Technology, London). Examination of the deposits by electron diffraction showed that initially epitaxial growth occurred, but that in some cases this was accompanied by rotational disorientation.

The smoothing of electrode surfaces by anodic dissolution or cathodic deposition was discussed by J. Edwards (British Non-Ferrous Metals Research Association), who showed how the potential distribution, hence the rate of solution or deposition, was influenced by the topography of the electrode surface.

The papers on internal surfaces were introduced by J. Nutting (University of Cambridge). He outlined first the forms of internal surfaces thought to exist in pure metals, single-phase and two-phase alloys, and then discussed in more detail the structure of interphase interfaces. New results, obtained by transmission electron microscopy of thin metal foils, on the coherent interfaces found in aluminium alloys after suitable aging treatments were described, and the transition from coherent to partially coherent interfaces was shown to occur by the introduction of suitable structural dislocations.

The properties of grain boundaries are frequently discussed, but not often measured. An attempt to obtain quantitative information was described by G. M. Leak (British Iron and Steel Research Association, Sheffield), who showed how the dependence of temperature of the internal friction of iron could be related to its grain size. The relaxation time of the grain boundary damping was also found to be dependent upon alloy content, different results being obtained with interstitial and substitutional elements. P. B. Hirsch and M. J. Whelan (University of Cambridge) and R. Bullough (Associated Electrical Industries, Aldermaston) were more concerned with low-energy interfaces associated with deformation twins. Drs. Hirsch and Whelan described a mechanism for the formation of deformation twins and then discussed this in relation to the contrast effects obtained when examining thin metal foils of stainless steel in the electron microscope, while Dr. Bullough presented a theoretical treatment of the properties of structural dislocations and their movement during the extension of a twin interface.

A series of papers on the influence of interphase interfaces upon the mechanical properties of alloys were then presented. Experiments on the plastic deformation of aged aluminium–copper and aluminium–silver alloys were described by A. Kelly (University of Cambridge), who showed that after aging an aluminium–copper alloy to produce *G.P.* [1] zones the critical resolved shear stress at a given elongation was very sensitive to temperature, whereas after aging to produce *G.P.* [2] zones, or the spherical zones in aluminium–silver alloys, there was no thermally activated component. He deduced from these results that, with the aid of thermal fluctuations, dislocations could be made to pass through the narrow

G.P. [1] zones, but with the larger and thicker *G.P.* [2] zones thermal activation could never provide sufficient energy for the disruption of the zones. The mechanism of hardening in aluminium–copper alloys was discussed further by D. Dew-Hughes and W. D. Robertson (Yale University). They carried out tensile tests on single crystals of alloys which contained between 1 and 5 per cent copper and which had been aged at different temperatures and then used the results obtained to test the predictions of Orowan, Fisher Hart and Pry on the relationships between the shear stress and the particle spacing. The conclusion was reached that a modification of the Fisher Hart and Pry relationship gave agreement between the observed and calculated results. To account fully for the effects of aging upon the critical resolved shear stress, Dew-Hughes and Robertson derived the stresses required to force dislocations through the solid solution, then to pull them through the coherent strain fields surrounding the zones and finally to disrupt the zones. The sum of these three component stresses agreed closely with the observed shear stresses.

The conclusions of Kelly and of Dew-Hughes and Robertson on the modes of dislocation precipitate interactions were supported by the results presented by G. Thomas and R. B. Nicholson (University of Cambridge). They examined in the electron microscope thin foils of suitably aged aluminium alloys and observed how the dislocations interacted with coherent, partially coherent and incoherent precipitates. Clear evidence for the passage of dislocations through coherent and partially coherent precipitates was presented. But there was little evidence for the dislocation loops forming around precipitate particles as predicted by Fisher Hart and Pry. Further results on precipitate – dislocation interaction were given by E. Smith (Associated Electrical Industries, Aldermaston), who described the effects of hydride precipitates upon the plastic deformation of titanium and showed how the reversible twinning found in pure titanium was hindered by the hydride precipitates. Under conditions of rapid loading cracks developed from the interface between the hydride and the hindered twin.

The generation of dislocations at incoherent interfaces was discussed by J. W. Mitchell and A. S. Parasnis (University of Bristol). They showed how, in a dispersion of glass spheres in silver chloride, the stresses developed at interfaces due to differences in thermal contraction of the two phases could lead to the formation of dislocations by a process of prismatic punching. Optical micrographs were shown of the dislocation loops and their spatial distribution within the silver chloride matrix. Another function of interfaces, as a source of vacancies, was demonstrated by R. S. Barnes (Atomic Energy Research Establishment, Harwell) and Prof. A. H. Cottrell (University of Cambridge), who had investigated the effects associated with the annealing of radiation damage in copper produced by bombardment with α-particles. They found small bubbles were produced on annealing and reasoned that these were formed by the diffusion and aggregation of vacancies from either the nearest free surface or internal surfaces such as large-angle grain boundaries; convincing proof that twin interfaces did not act as sources for vacancies was produced. The influence of curvature on the energy of incoherent interfaces was illustrated by a film presented by G. Thomas and M. J. Whelan (University of Cambridge). Thin foils of an aluminium – 4 per cent copper alloy were aged at temperatures between 350° and 450° C. on a heating stage in the electron microscope while the structural changes as observed on the fluorescent screen of the microscope were recorded with a ciné camera. The nucleation and growth of the θ phase was clearly revealed together with the subsequent growth of the larger particles at the expense of the smaller ones.

From the conference it appeared that at the present stage of development the physicists and metallurgists had more to offer than the physical chemists towards our understanding of interfacial phenomena. The advances made since the introduction of electron diffraction techniques for the study of surfaces have been very great, but with the advent of the electron microscope into this field of study a much more detailed investigation of surface morphology has become possible. The explanation of why diffraction patterns could be obtained from deposits of less than one atom mean thickness has now been found, but it is still difficult to account for the preferential formation of epitaxial nuclei at lattice defects. Perhaps it is here that the physical chemists can be of help.

J. Nutting

THE COLOMBO PLAN

ANNUAL REPORT

THE seventh annual report of the Consultative Committee for the Colombo Plan for Co-operative Economic Development in South and South-East Asia, which by agreement at the Singapore meeting of the Committee in October 1955 has been extended from July 1957 to June 30, 1961, is the last to appear before the future of the Plan is again considered at its 1959 meeting in Indonesia. The present report*, which covers the year 1957–58, records continuing increase in industrial production in the area as a whole, but in India the rate of expansion dropped from 8 per cent in 1956–57 to 1·5 per cent, which, however, accounted for most of the 13 per cent increase in output of electric power. Since 1950 training has been given to more than 15,500 trainees from countries in the area, and the services of nearly 8,000 experts provided by members of the Colombo Plan and by agencies of the United Nations. During 1957 expenditure on technical assistance under the Colombo Plan Technical Co-operation Scheme increased to about £3 million, reaching a total of £9·78 million since 1950, and during the first six months of 1958 it reached 3·9 million dollars.

Almost half of this expenditure has been for the provision of study and training courses, about a quarter for the supply of experts and the remainder on technical equipment. By the end of June 1958 expenditure on technical equipment reached a total of £2·35 million, and the number of scholarships and training awards granted by member countries totalled 6,952, an increase of 1,330 on the previous year.

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* The Colombo Plan for Co-operative Economic Development in South and South-East Asia—Seventh Annual Report of the Consultative Committee, Seattle, Washington, November 1958. Pp. 192. (Cmnd. 610.) (London: H.M. Stationery Office, 1958.) 8*s*. net.

There were then 2,091 trainees taking courses in member countries. During the year there were 221 technical experts in the field compared with 207 in the previous year, making a total of 1,002 since the Plan began. The number of experts supplied in medical and health fields dropped sharply, but the number of engineering experts increased, and the number of those in food, agriculture and forestry and in transport and communications continued to increase.

Outside the Technical Co-operation Scheme, the United States, which has already provided, since the inception of the Plan, almost 4,000 million dollars in economic and technical assistance to Colombo Plan countries, continued to provide large-scale technical assistance. About 1,500 trainees were received in the United States and 543 trainees undertook instructional courses with United States assistance in the Colombo Plan area, while on July 1, 1958, about 2,000 United States technicians were on duty in Colombo Plan countries. Under the Mutual Security Programme and the President's Fund for Asian Economic Development, 408 million dollars were made available to Colombo Plan countries during the year, and finance was provided for a Radioisotope Centre in Burma, including arrangements to train Burmese in nuclear techniques in the United States. Laboratory equipment was provided for a course in nuclear physics at the University of the Philippines, and scientists from the Philippines and Thailand are being trained in the United States.

During the year, fewer new Colombo Plan scholarships and training awards were granted, partly because of the pressure on existing training institutions but partly also because of the marked increase in the number of long-term awards. The establishment and development of training facilities within the area accelerated and 20 per cent of the training awards under the Technical Co-operation Scheme are now provided within the area. Looking to the future, the report again stresses the need to ensure that technical and managerial skills are developed at a rate sufficient to permit the effective use of capital and other available resources. The technical ability of the population must keep pace with the expansion of development and it is now urged that the less-developed countries give greater attention to the development of human skills required for the effective and appropriate utilization of resources. Finally, stress is laid both on the value of co-operation and of the more rapid development of technical training facilities within the area.

BEAR ISLAND COD

DURING the summer, shoals of cod, consisting mainly of immature individuals, move into feeding grounds off Bear Island near Spitsbergen. These concentrations form an important fishery resource, and for the past ten years, part of the work of the Fisheries Laboratory, Lowestoft, has been to trace the migrations that lead to this shoaling behaviour.

In doing this work*, Mr. G. C. Trout has been greatly helped by discovering that these cod have two main kinds of otoliths, which he calls split-zone and opaque-zone types. Both kinds are found in roughly equal proportions on the more southerly grounds, but with increasing distance from Bear Island the two tend to become segregated. This and other evidence suggested that the shoals advancing on Bear Island separate into two groups, one moving north-eastwards in the direction of Hope Island and the other northwards to Spitsbergen. Tagging experiments carried out during 1951 and 1952 were in keeping with this hypothesis and showed that in late autumn the fish returned to winter quarters in the Bear Island area.

Trout suggests that these facts and others are consistent with the general idea that the annual migratory cycle of the Barents Sea cod populations is closely linked with the movements of the water masses. During their summer migrations the feeding cod are partly pelagic in habit (due to daily vertical migrations in response to light conditions) and may thus drift northwards in the West Spitsbergen current or in a branch of the North Atlantic drift. The return migration in winter is against the current and takes place along the bottom in the absence of light (and the lack of daily vertical movement in the fish). The distribution of the cod is thus seen to be ". . . the resultant of interaction of changing behaviour with the cycle of movement of the water masses in which the cod are found".

This would seem to be a useful working hypothesis. Perhaps it will prove to be partly right, but the fact that it can be posed at all is a measure of the work being undertaken by the Fisheries Laboratory at Lowestoft.

N. B. MARSHALL

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* The Bear Island Cod: Migrations and Movements. By G. C. Trout. Fishery Investigations, Series II, Vol. 21, No. 6. Pp. 51. (London: H.M. Stationery Office, 1957.) 16*s*.

PROGRESS IN BRITISH FORESTRY

THE thirty-eighth annual report of the Forestry Commissioners for the year ending September 30, 1957*, reviews both the record of work accomplished in Britain and the national situation in relation to policy and programmes adopted by the Government. The record as a whole must be accepted as quite satisfactory, with encouraging features indicating that some at least of long-standing difficulties are being overcome, even if others, such as that of acquiring land for afforestation, have definitely held up progress in planting work. Criticism has been made in the past that not enough was being done to get the productivity of the privately owned woodlands—still the greater proportion over the country as a whole and still far from having recovered from the onslaught of two world wars—restored and brought up to the levels possible with skilled management. The rate of planting by private owners has nearly doubled in the past five years and has increased by as much as 4,500 acres in 1956–57, compensating for a drop of the same order in the State's own total. This increase is significant as revealing a changed situation which has been widely discussed, both in

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* Thirty-eighth Annual Report of the Forestry Commissioners for the year ended 30th September, 1957. Pp. 90+4 plates. (London: H.M. Stationery Office, 1958.) 5*s*. 6*d*. net.

Parliament and among foresters, and one to which the Zuckerman Report also directed attention.

The national policy since the end of the First World War has been to build up a stock of standing timber estimated to be adequate to make Great Britain independent of imports of wood over an emergency lasting about five years, and the question is naturally being asked whether, with the changed conditions now prevailing, we should still continue to retain the same target of 5 million acres of productive forest. Although it can be demonstrated that there is still enough suitable land, there are practical difficulties in acquiring it, and, of course, afforestation implies a large capital investment at a time when there are innumerable demands for capital. Forestry is unquestionably becoming more attractive to the private investor despite the current drop in prices, while the Government is also tending to place the emphasis on the economic and social benefits of forestry rather than on the earlier strategic reasons.

An important factor is certainly that more and more of the new forests in Britain are coming into production, often large-scale production, and it is obvious that the annual output is going to rise steadily for as many years to come as we have maintained a large planting programme. Not only is this giving more and more local employment, but also one centre after another is seeing new industrial units open up, or existing ones expanding: in the year under report, this has happened in Flintshire, Lancashire, Dumfriesshire and Monmouthshire, and this is clearly only a beginning. It is noteworthy, too, that 400 miles of new roads have been completed, with 313 more under construction, reducing the inaccessibility to modern amenities that has hitherto contributed so much to rural depopulation. The only other feature of this report which can be referred to here is the attention given to developing the social aspects of forestry, particularly in connexion with the national forestry parks, which all record very significant increases in the numbers of visitors and for which an excellent series of small guides has been issued. The special importance of awakening an interest in forestry among the rising generation is receiving recognition in the form of the provision of facilities in the forests for schools and for colleges for the training of teachers.

H. G. CHAMPION

FORMATION OF ABERRANT CELL WALLS AND OF SPORES BY THE GROWING YEAST PROTOPLAST

By A. A. EDDY* and D. H. WILLIAMSON
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THE so-called protoplasts which have been isolated by exposing various micro-organisms to conditions favouring dissolution of the cell wall may be placed in two main categories depending on their ability or inability to reform a normal cell wall on cultivation and thereby to revert directly to cells of the parent type[1]. Work in these laboratories with protoplast-like bodies released from yeast by the action of gut-juice from *Helix pomatia*[2] has now brought to light the interesting situation that, whereas they have never been observed directly to revert to whole cells, they nevertheless are capable of giving rise to a superficial membrane which, to some extent, resembles the normal wall of the yeast cell. However,

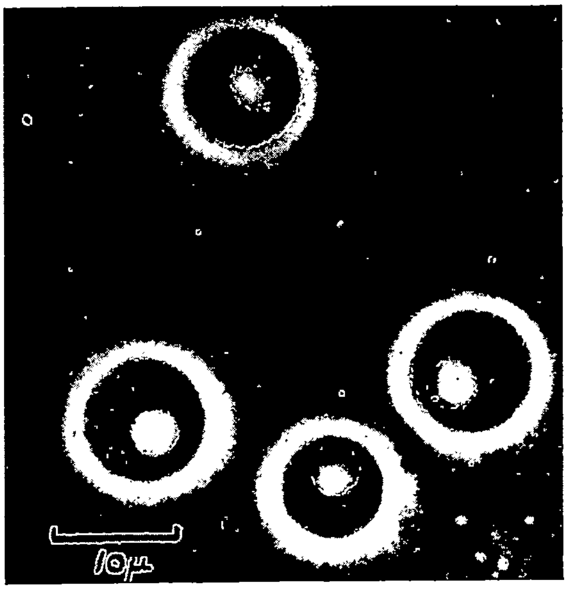


Fig. 1. Freshly isolated protoplasts

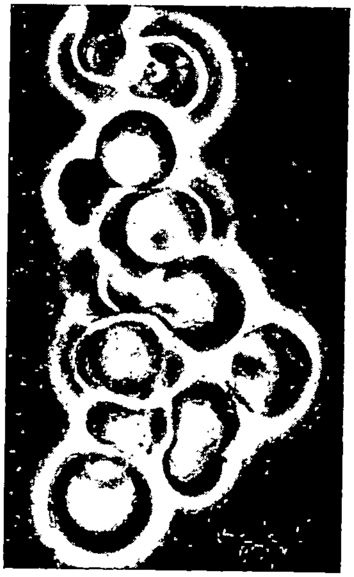


Fig. 2. Protoplasts suspended for 2 hr. at 25° C. in malt extract medium (ref. 3) containing 10 per cent (w/v) glucose

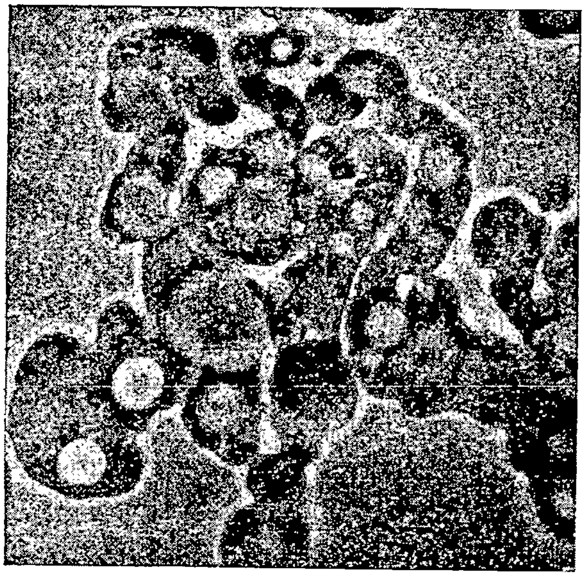


Fig. 3. Protoplasts after incubation for 40 hr. at 25° C. on solid malt extract medium (ref. 3) containing 10 per cent (w/v) mannitol

conditions have been found which induce the protoplasts to form spores from which whole cells may arise on germination, the process thus providing an indirect means of effecting reversion to the normal state.

The method of isolating protoplasts was modified from that previously described[2]: (1) by using mannitol as an osmotic stabilizer instead of rhamnose; (2) by effecting solution of the wall at 30° C. rather than at 25° C.; (3) by using 5 mgm./ml. instead of 1 mgm./ml. of snail enzyme. Under these conditions, more than 90 per cent of the cells of *Saccharomyces carlsbergensis* (National Collection of Yeast Cultures, strain 74) were converted into protoplasts in 2–3 hr., the product containing not more than 0·1 per cent viable whole cells as determined by plating it on a solid medium lacking mannitol.

Samples of protoplasts (10^7–10^8/ml., final concentration) were transferred to a series of nutrient media which were either based on malt extract[3] or were of the synthetic type[4]. The media were supplemented with either mannitol, glucose, maltose or sucrose at selected concentrations equivalent to osmotic pressures of 10–20 atm. When malt-extract was used, aureomycin (20 μgm./ml.) was included to suppress growth of bacteria. Examination of samples withdrawn at intervals from cultures variously held at 18–30° C. for periods of up to 2 weeks revealed that the protoplasts underwent a sequence of striking changes in appearance. For example, 1–2 hr. after transfer to a complete growth medium, the surfaces of the protoplasts displayed irregular local swellings (Figs. 1 and 2) which, during a subsequent 30 hr., tended to develop into massive irregularly shaped outgrowths (Fig. 3), the protoplasts themselves increasing 5–50 fold in volume. That a form of growth was involved in these changes was readily demonstrated by showing that the respective contents of protein, ribonucleic acid and insoluble anthrone-positive carbohydrate, determined by conventional methods, increased several-fold during the first few hours.

The way in which swelling of the growing protoplasts occurred suggested the presence of a fairly rigid membrane defining the outline of the cell at each stage of growth. In fact, such membranes

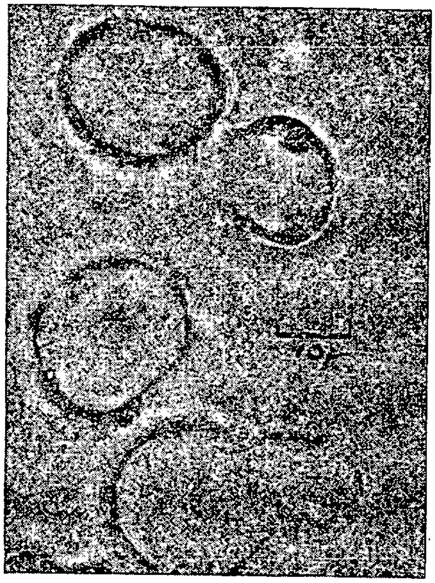


Fig. 4a. Aberrant cell walls (phase contrast)

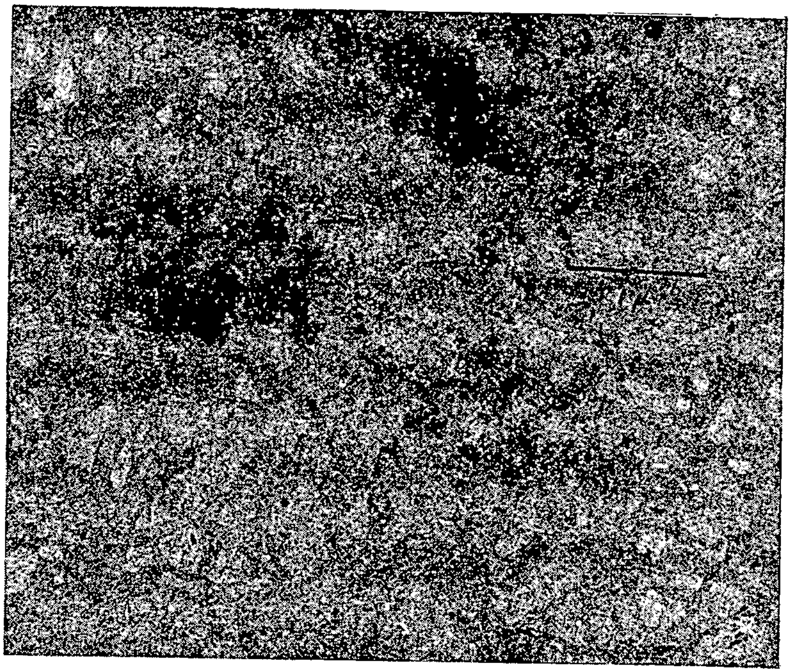


Fig. 4b. Aberrant cell walls (unshadowed electron micrograph)

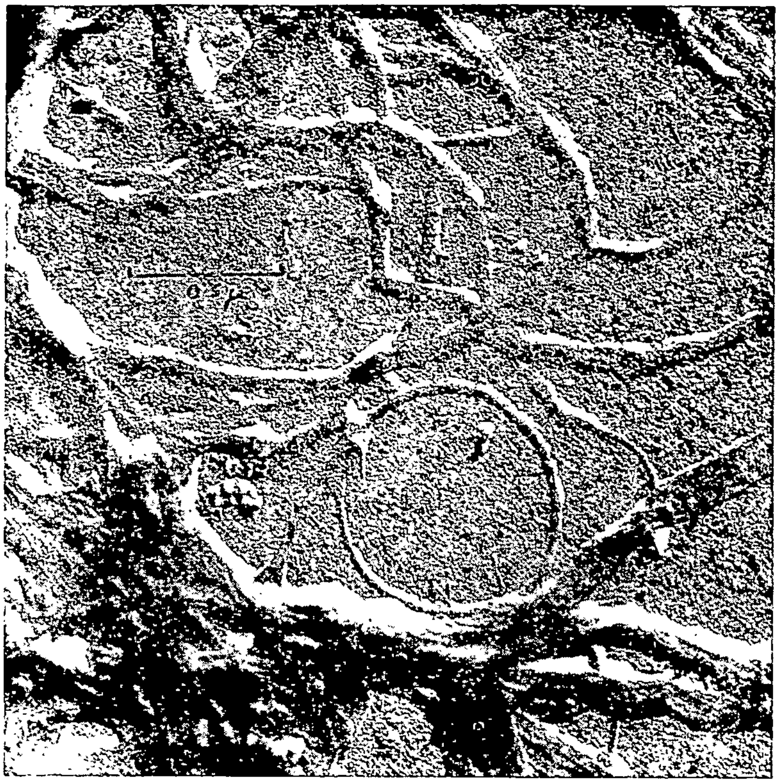


Fig. 4c. Aberrant cell walls (shadowed electron micrograph)

were present and could readily be detected on adding an excess of water (10 vol.), which caused the contents of the protoplasts to disperse while the outer envelopes were preserved. No trace of the membranes was found, however, when freshly isolated protoplasts were lysed in this way.

In order to examine them further, the membranes released by lysis were centrifuged at 1,000*g* for 5 min. and washed with water. They were then shaken for 10 min. with fine glass beads in a Mickle disintegrator in order to remove adhering debris, and recovered once more by centrifugation. The form and fine structure of the membranes are illustrated in Fig. 4*a*, *b* and *c* (electron micrographs obtained by courtesy of Metropolitan Vickers, Ltd.), respectively, while their composition is contrasted in Table 1 with that of normal walls derived from the same strain of yeast.

A striking feature of the composition of the material comprising the aberrant walls is its relative deficiency in amino-acid residues, most of the nitrogen content, in fact, being accounted for as N-acetylglucosamine. This circumstance may be attributed to the absence from the surface of the protoplast of a specific protein template which, in the case of the intact cell, plays a direct part in the synthesis of new cell wall material. In these terms, the aberrant walls can perhaps be regarded as representing part of the basic structure of the normal wall.

The results obtained on culturing the protoplasts in synthetic medium deficient in available nitrogen were quite different from those described above in that little or no irregular

Table 1. COMPARISON OF CELL WALLS PRODUCED BY THE PROTOPLAST WITH THOSE FROM THE PARENT YEAST

	Nitrogen (per cent dry wt.)	Phosphorus (per cent dry wt.)	N-acetyl glucosamine* (per cent dry wt.)	Invertase† (μmole sucrose/mgm. wall/hr.)
Normal cell wall	1·0	0·19	0·9	6
Protoplast wall**	2·2–2·7	0·03	27–33	≮ 0·03
	Amino-acids	**Mannose‡**	**Glucose‡**	**Anthrone-positive§ carbohydrate (per cent dry wt.)**
Normal cell wall	+++	+	++	55
Protoplast wall**	±	+	++	35–45

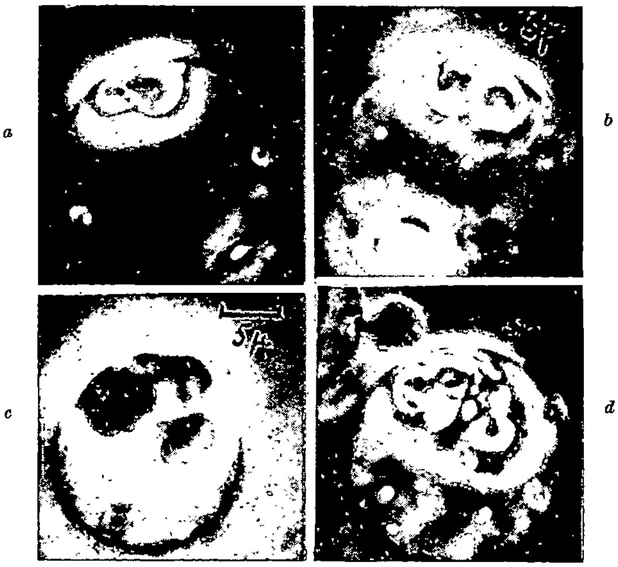
* Determined after hydrolysis for 72 hr. with two successive portions of snail enzyme (ref. 7).

† Measured at 25° C. in presence of 0·01 *M* acetate buffer, *p*H 5·3. Activity of normal walls was shown to be twenty times greater than could be accounted for by the proportion of whole cells present.

‡ Found after hydrolysis with sulphuric acid (70 per cent v/v) for 2 hr. (ref. 7).

§ Calculated as glucose equivalent.

** Values refer to three independent preparations.



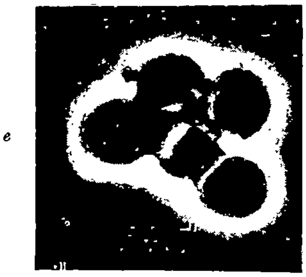


Fig. 5*a–d*. Spores forming within protoplasts held for 40 hr. at 25° C. in a synthetic medium (ref. 4) from which ammonium sulphate was omitted, supplemented with 0·1 per cent (w/v) glucose and 10 per cent (w/v) mannitol at *p*H 6·5. *e*, a cluster of spores released by diluting such a culture

swelling of the protoplasts occurred. They tended instead to develop a large main vacuole at the perimeter of which, and still within the protoplast itself, a cluster of 2–5 highly refractile spherical bodies each of about 3μ diameter could be discerned (Fig. 5). The appearance of these refractile bodies, their ability to develop into mixtures of haploid and diploid cells on being transferred to nutrient media of low osmotic pressure, as well as their reaction to the spore stain of Bouthilet[5], strongly suggested that they were, in fact, spores in various stages of development. In this connexion, it may be significant that culture of the parent yeast itself in a similar nitrogen-deficient medium also resulted in a good yield of ascospores being obtained.

It is stressed that throughout this work no evidence was obtained that the yeast protoplasts were able to produce intact cells other than through spores as an intermediate stage. This conclusion is apparently at variance with the work of Nečas[6], who claimed to have observed direct development of yeast cells from protoplast-like bodies originally obtained from a spontaneously lysing yeast. While this author seems to have encountered material such as that illustrated in Fig. 3, he apparently failed to detect development of aberrant cell walls. It is interesting to speculate that, under the conditions employed by Nečas, spores may have been formed and have germinated so rapidly that their presence was not detected. In this connexion it may be significant that Nečas found regenerated yeast cells to differ both among themselves and from the parent strain, an observation which would be compatible with their having *originated* from different spore segregants.

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[1] Weibull, C., "Ann. Rev. Microbiol.", 12, 1 (1958).
[2] Eddy, A. A., and Williamson, D. H., *Nature*, 179, 1252 (1957).
[3] Wickerham, L. J., Tech. Bull. U.S. Dept. Agric. No. 1029 (1951).
[4] Kilkenny, B. C., and Hinshelwood, Sir Cyril, *Proc. Roy. Soc.*, B, 139, 73 (1951).
[5] Phaff, H. J., and Mrak, E. M., *Wallerstein Lab. Commun.*, 11, 261 (1948).
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[7] Eddy, A. A., *Proc. Roy. Soc.*, B, 149, 425 (1958).

CÆSIUM-137 IN SWEDISH MILK AND SOIL

By K. LÖW and K. EDVARSON
Research Institute of National Defence, 2nd Division, Stockholm 80

THE cæsium-137 content of dried milk from mid-Sweden and in soils from different locations has been determined by γ-spectrometric methods. One dried milk sample was from 1947, the others from 1955–58 (kindly provided by Svenska Mjölkprodukter AB, Stockholm). The soils were sampled in the summer of 1957. Three samples, consisting of the layers 0–2·5, 2·5–5 and 5–10 cm. were taken at each place.

Cæsium-137 was determined directly by γ-spectrometry without chemical separation. The detector was a 4 in. × 4 in. sodium iodide (thallium) crystal, made by Harshaw Chemical Co., with copper housing and 'Pyrex' window. To get a high geometrical efficiency the sample container made of thin copper sheet was so shaped that the sample formed a layer of uniform thickness around the crystal (cf. Fig. 1). The volume of the container was 0·7 l., corresponding to about 500 gm. dried milk and 600–1,000 gm. soil. The detector unit was surrounded by a 10-cm. lead shield. The pulse analyser was of the Hutchinson-Scarrot type with 70 channels and was used with a channel-width of 25 keV.

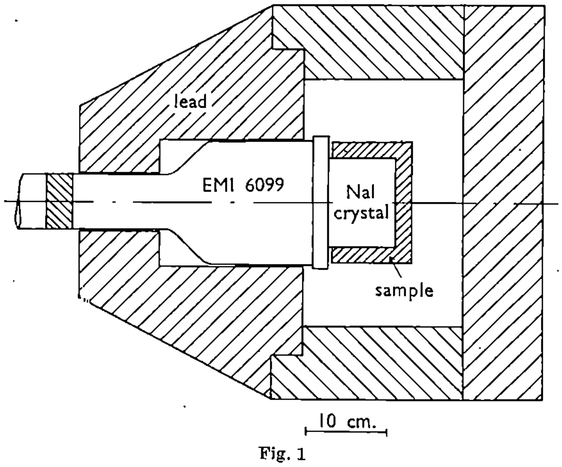

Fig. 1

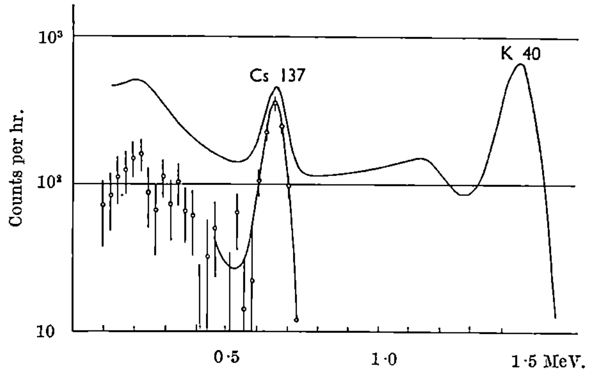

Fig. 2. Dried milk

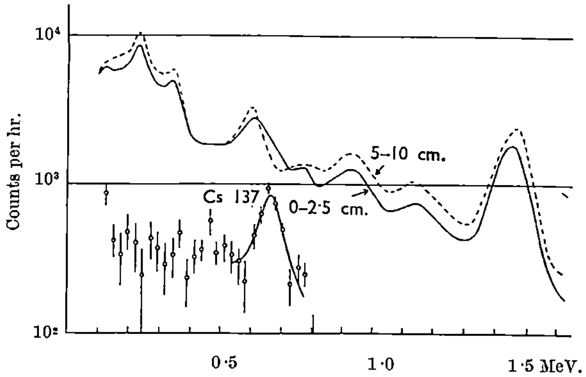

Fig. 3. Soil No. 4

Table 1. CÆSIUM-137 AND STRONTIUM-90 IN MILK

(1) No.	(2) Date of manufacture	(3) pc. Cs-137/gm. K	(4) pc. Cs-137/l. milk	(5) pc. Sr-90/gm. Ca	(6) pc. Sr-90/l. milk	(3)/(5)	(4)/(6)
1 W*	28.8.47	< 1	—	< 0·14	—	—	—
2 W	29.11.55	17·0	27	2·50	2·7	6·8	10·2
3 S	14.2.56	12·1	20	1·70	1·9	7·1	10·6
4 W	24.4.56	12·2	18	1·98	2·1	6·2	8·8
5 W	22.10.56	28·3	42	4·32	4·5	6·6	9·3
6 W	6.1.57	17·0	26	3·37	3·6	5·1	7·1
7 S	1.6.57	18·8	26	4·54	4·1	4·1	6·3
8 W	21.6.57	22·1	34	3·87	4·0	5·7	8·4
9 S	15.9.57	53·1	77	6·37	7·3	8·3	10·6
10 W	13.12.57	22·4	33	4·88	5·3	4·6	6·2
11 S	21.1.58	22·6	37	4·47	5·2	5·1	7·1
					Mean	6·0	8·5

* W, whole milk; S, skimmed milk. The estimated errors are: col. 3, ± 1; col. 5, ± 0·1.

The only detectable γ-activity in the milk was due to cæsium-137 and potassium-40. A typical γ-spectrum of dried milk is shown in Fig. 2. The absolute efficiencies and the shape of the spectra of these activities were determined by measuring milk samples with known amounts of cæsium-137 and potassium added. The lower curve in Fig. 2 was obtained by subtracting the potassium contribution, determined from the 1·45-MeV. photopeak. The shape of this curve fits well with the cæsium-137 spectrum determined in the calibration. A counting time of 2 hr. gives a statistical error of 5–10 per cent in the determination of cæsium at the present levels of milk activity (~ 20 pc./gm. potassium).

In the soils, the cæsium-137 activity could not be determined directly because of the radium and thorium content. In particular, the 0·61-MeV. line due to radium C, which is of high intensity and is close to the 0·66-MeV. line due to cæsium-137, interferes.

There is reason for believing that the cæsium-137 content in the 5–10 cm. layer is much lower than that in the upper layers, whereas the composition of the natural activity (thorium, radium, potassium) might be about the same for the three layers. Thus it would be possible to determine cæsium-137 from the difference in γ-spectra between a top layer and the bottom layer. In Fig. 3 the γ-spectra from the 0–2·5-cm. and 5–10 cm. layers of one soil are given. Above 0·8 MeV. the shapes of the spectra are the same within the statistical errors, indicating that the relative amounts of the components of the natural activity are the same. By normalizing the spectrum of the bottom layer to give the same intensity above 0·8 MeV. as the upper layer and subtracting it from the latter, a residue was obtained mainly consisting of a well-resolved cæsium-137 peak. Clearly, the amount of cæsium-137 in the bottom layer must be very small compared with the upper layer if this method is to give the true content of cæsium-137. The known behaviour of cæsium tracer in soils[1] indicates that this assumption is justified. The same calibration as for dried milk was used, because the difference in density and composition between soil and dried milk is estimated to be of small importance with the present geometry. With a counting time of 1 hr. the error in the cæsium-137 determination is estimated to be ± 40 pc./kgm. soil at the present low levels of activity.

Table 2. SOIL TYPES AND PRECIPITATION-RATES

No.	Location	Type of soil	Yearly precipitation-rate (mm.) Mean 1955–57
1	Skarhult 55·9° N., 13·3° E.	Moraine loam	570
2	Fröslida 56·8° N., 13·0° E.	Fine sand	1,180
3	Ultuna 59·8° N., 17·7° E.	Heavy clay	530
4	Offer 63·0° N., 18·0° E.	Silty clay loam	500

Measurements on soils sampled during the summer of 1958 were started in August 1958. In this case the main γ-activity in the top layer is due to zirconium + niobium-95 (0·75 MeV.) in fall-out during the first half of 1958. It is estimated that a determination of cæsium-137 for these soils will be possible in 1959, when the zirconium + niobium-95 has decayed sufficiently.

(*a*) *Milk.* The results are given in Table 1. For comparison the content of strontium-90, determined radiochemically by S. Häggroth[2], is also given. As is to be expected, the sample from 1947 contains no detectable cæsium-137 or strontium-90 activity. It is not possible with the present material to find any trend as regards the variation with time in the other values. The correlation between cæsium-137 and strontium-90 is, however, quite good. Assuming a linear dependence, the coefficients of correlation are 0·84 and 0·91 for columns 2–5 and 4–6 respectively.

(*b*) *Soil.* Some characteristics of the soils are given in Table 2 and the results are summarized in Table 3. The amounts of activity seem to be in reasonable agreement with measurements of activity

Table 3. CÆSIUM-137 AND STRONTIUM-90 IN SOILS

(1) Soil No.	(2) Layer	(3) pc. Cs-137/ kgm. soil	(4) mc. Cs-137/ $km.^2$	(5) pc. Sr-90/ kgm. soil	(6) mc. Sr-90/ $km.^3$	(4)/(6)
1	0–2·5	1,450	35·9	574	14·2	
	2·5–5	126	3·5	66	1·8	
	5–10	0*		18	1·1	
			39·4		17·1	2·30
2	0–2·5	574	15·9	210	5·8	
	2·5–5	125	3·3	74	2·0	
	5–10	0*		22	1·2	
			19·2		9·0	2·14
3	0–2·5	447	12·5	216	6·0	
	2·5–5	0	0·0	57	2·0	
	5–10	0*		16	1·0	
			12·5		9·0	1·40
4	0–2·5	570	13·1	202	4·7	
	2·5–5	0	0·0	22	0·5	
	5–10	0*		4·5	0·3	
			13·1		5·5	2·38

* Assumed value.

The estimated errors of the sums for each soil are ± 1·5 in col. 4 and ± (0·1–0·3) in col. 6.

in precipitation[3]. A detailed comparison is not possible until more extensive material is available. The ratio cæsium/strontium is in fair agreement with measurements made by N. G. Stewart *et al.*[4].

The results indicate that there is a good correlation between the cæsium-137 and strontium-90 values not only in soils, where it is to be expected, but also in milk. It is of course quite probable that regions with different climatic and agricultural conditions will give milk with different ratios of cæsium-137 to strontium-90, but within each region it seems possible to use the cæsium-137 values for an estimation of the strontium-90 content, provided that the contamination is due to atomic bomb debris. As the determination of cæsium-137 is far more rapid than the radiochemical determination of strontium-90, this would have practical advantages.

As regards the soils, the direct determination of cæsium is of special value, as the present radiochemical methods for the determination of strontium-90 mostly involve an extraction of the soil, the efficiency of which it is extremely difficult to determine.

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HAIR RECEPTORS IN LOCUSTS

Hair Plates on the First Cervical Sclerites of the Orthoptera

MITTELSTAEDT[1] has described four pairs of hair plates in the neck of the dragonfly, *Anax imperator*, which register movement of the head relative to the body. A pair of hair plates found in the neck of the locusts *Schistocerca gregaria* and *Locusta migratoria migratorioides* (Fig. 1) has been shown to fulfil a similar function. The tip of the first cervical sclerite on each side of the neck bears an oval swelling covered with fine hairs (Fig. 2) at the point where it forms a ball-and-socket joint with the post-occipital condyle of the head. Several types of head movement, in particular rotation of the head relative to the long axis of the body, deflect these hairs and also some, at least, of the hairs on the anterior edge of the prothorax. The hair plate is innervated by a branch of the second pair of nerves from the first thoracic ganglion; a second branch of this nerve runs up to the anterior edge of the prothorax.

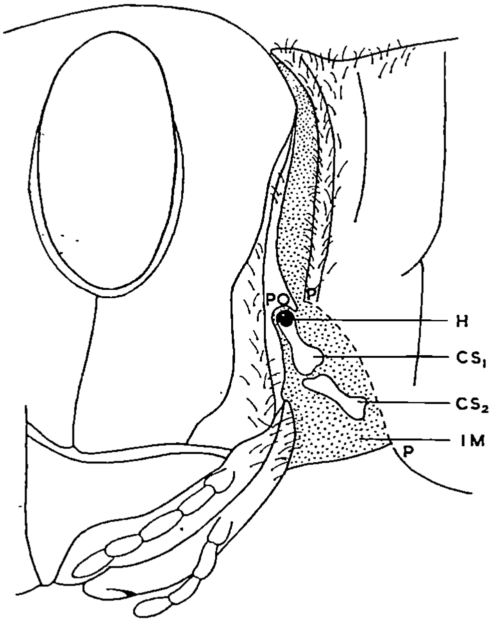

Fig. 1. Diagram of part of the head and prothorax of *Schistocerca gregaria* with the head pulled slightly to one side to reveal the intersegmental membrane, cervical sclerites and hair plate. Some of the hairs present on the prothorax and head are also shown. *P–P*, pronotum cut away to reveal the cervical sclerites; CS_1, CS_2, first and second cervical sclerites; the second sclerite articulates with the region of the pronotum that has been removed; *H*, hair plate; *PO*, post-occipital region of the head; *IM*, intersegmental membrane

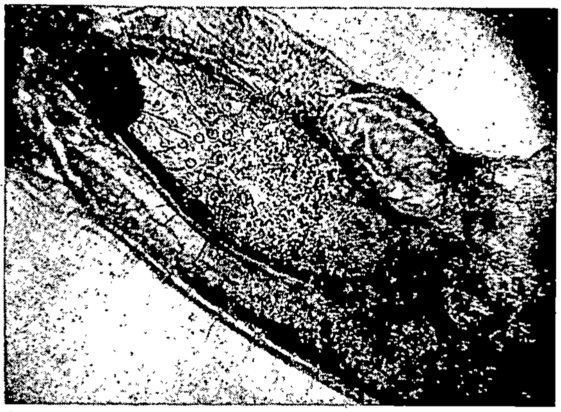

Fig. 2. A photograph of the tip of the first cervical sclerite, showing the oval swelling of the hair plate bearing many fine hairs

Laboratory studies with flying locusts have demonstrated that *Schistocerca* and *Locusta* show a dorsal light reaction, similar to that shown by *Anax*, turning about the longitudinal axis until the greatest light-intensity falls on the dorsal ommatidia, then continuing to fly in this position. The head is turned until the dorsal ommatidia are perpendicular to the light source and the body is then rotated to be aligned with the head. The ability of the locust to remain thus orientated is reduced if all the hairs on the anterior edge of the prothorax are destroyed, and it is extremely difficult for it to do so if the hair plates are destroyed. If both the hair plates and the prothoracic hairs are destroyed the locust still rotates until the dorsal ommatidia are perpendicular to the light source but is completely unable to remain orientated in this position because the body cannot be maintained in the correct angular position relative to the head. The hair plates, and to a lesser extent some of the prothoracic hairs, function as proprioceptors registering relative head and body movement.

Hair plates have been found on the first cervical sclerites of representatives of all the main families of Saltatoria. They are present in flightless subterranean species such as *Gryllotalpa gryllotalpa* and *Cylindracheta* sp., in brachypterous species like

Pholidoptera griseoaptera, and in wingless forms such as *Lentula callani*, as well as in alate species such as *Chorthippus brunneus*. They are well developed in nymphs as well as adults and it seems likely that they have a similar proprioceptive function throughout the order.

This work was carried out during the tenure of a Senior Research Award from the Anti-Locust Research Centre, London.

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Function of certain Prothoracic Hair Receptors in the Desert Locust

The behavioural experiments of Goodman (previous communication) suggest that registration of displacement of the head relative to the body—particularly rotational movement—in *Schistocerca gregaria* is carried out at least in part by external proprioceptors, consisting of hair sensillæ on the cervical hair plates and on the anterior edge of the pronotum. This view would be corroborated if the responses of the hairs were found to be those typical of other insect hair proprioceptors, such as those described by Pumphrey[1] and Pringle[2].

Attempts were therefore made to record the electrical discharges in the nerves supplying these hair receptors while the latter were stimulated with a mechanically controlled glass needle. The hairs are innervated by branches of the second nerve of the first thoracic ganglion; using fine platinum wire electrodes and a high-impedance input d.c. amplifier, it proved impossible to record discharges in the nerves supplying the cervical hair plates, which were so fine that the necessary dissection either broke them or caused them to dry out rapidly. It was possible, however, to record discharges in the nerve supplying the hair sensillæ distributed along the anterior edge of the pronotum. A constant maintained deflexion of a single hair with a fine glass needle then produced a relatively high initial discharge frequency (200–300 impulses/sec.) which became adapted rather rapidly to a steady level of 40–50 impulses/sec., which was maintained for a long period (Fig. 1). The response was obtained to deflexion of the hairs in any direction and the initial frequency of discharge appeared to depend both on the speed and magnitude of the original deflexion; the adapted frequency, however, bore no relation to the magnitude of the deflexion, as Pumphrey[1] found in certain cockroach proprioceptors, and indeed this level was very similar in all preparations (Fig. 1). The hairs could be stimulated by gross air movements and also by pure tones in the range 100–500 c./s., if these were of sufficient intensity; in the latter case the response was synchronous with the stimulus frequency.

The responses described above are very similar to those found by Pumphrey[1] and Pringle[2] in certain insect hair sensillæ now agreed to be proprioceptors, and certainly fit the receptors for the role suggested for them by Goodman. The pronotal receptors on one side, up to the dorsal median line, are innervated by the nerve of that side; thus, with the two cervical hair plates, there are in all four hair beds, disposed in such a way that information about the equilibrium position and direction of rotation of the head relative to the body can be registered. It seems likely that the cervical plates register the equilibrium position, while the prothoracic hairs register movement; this speculation is supported by Goodman's evidence that removal of the cervical plates makes the maintenance of an equilibrium position almost impossible, while removal of the prothoracic organs only partially reduced this ability.

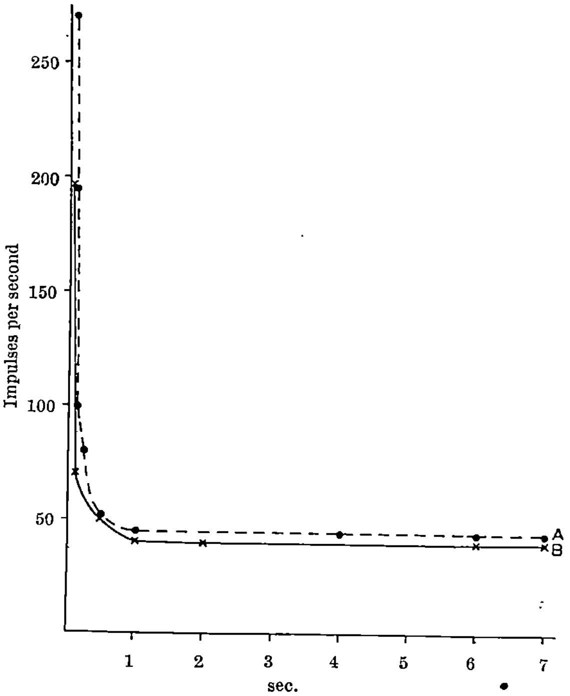

Fig. 1. Impulse frequency elicited by constant deflexion of single prothoracic hair receptor plotted against time after onset of stimulus; curve *A* resulted from a greater initial deflexion than for *B*

If the pronotal hair fringe is examined closely, it is found that it consists of a collar of upstanding, anteriorly sloped hairs which are only displaced by head movements in the dorso-ventral plane or by extreme angular rotations, and also a number of hairs on the underside of the edge of the pronotum which would appear to be displaced by any movement of the head relative to the body. Since the hairs in the collar-like fringe are deflected by wind when the locust is in flight, it would seem that proprioceptor functions in the air are carried out by the hairs under the edge of the pronotum. Histological preparations of the hairs (for which I am indebted to Miss K. M. Becker) show no apparent differentiation between the organs on the upper and under sides of the edge of the pronotum nor indeed from certain other, presumably tactile, hairs found elsewhere in the locust; the nerve fibre ending is apparently inserted at the centre of the hair, which accords with the fact that bending in any direction produces a response. This should be contrasted with the eccentric nerve insertion in campaniform sensillæ and in hairs responsive to bending only in one direction, noted by Pringle[3].

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Dec. 10.

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LETTERS TO THE EDITORS

CHEMISTRY

Enhancement of Radiation-induced Cross-linking of Polyvinyl Chloride

The beneficial effects of ionizing radiation on certain polymers are well known. In the case of thermoplastics, such as polyethylene and polyvinyl chloride (P.V.C.), radiation-induced cross-linking confers insolubility and infusibility. Moreover, the tensile strength, elastic modulus and resistance to swelling increase progressively with the density of cross-linking. Many published studies have shown that the latter is approximately proportional to the radiation dose and largely independent of other factors such as radiation intensity[1]. In practice, fairly substantial doses in the range 10^7–10^8 rads are necessary to produce high densities of cross-linking. Radiation doses in the upper range are undesirable however, not only because of the current high cost of sources of radiation, but also because cross-linking is commonly accompanied by dislinking and other side-reactions, giving rise to impurities which may accumulate with the dose. This feature is particularly troublesome with polyvinyl chloride, in which cross-linking is accompanied by dehydrochlorination and discoloration[2].

These difficulties were early realized and have led to a search for additives which would enhance the cross-linking reaction. A true sensitizer is one that would increase the primary yield of cross-links, that is to say, enhance the interaction of radiation with the polymer. Neither theory nor practice encourages confidence that such a sensitizer may emerge. It is known, however, that high densities of cross-linking result from low doses when there is a possibility of a chain-reaction, as in unsaturated polyesters[3]. There is no increase in yield of primary radicals, but several network junction points may be created for each initiating radical during the propagation reaction, and the density of cross-linking is no longer solely proportional to the radiation dose.

A chain reaction could also be exploited with normally saturated polymers, like polyvinyl chloride, if these could be induced to suffer chain-transfer with a suitable propagating monomer *in situ*, for each chain-transfer step could lead to an additional junction point on the polyvinyl chloride. Recent studies on the polymerization of allyl esters have shown that these have a short propagation chain-length due to degradative chain-transfer, but that this process is accompanied by effective chain-transfer[4]. Diallyl and triallyl esters, moreover, are readily available and are compatible with polyvinyl chloride.

The rate of polymerization of pure allyl esters under irradiation by electrons or by γ-rays was found to be very low, compared with vinyl esters (Pinner, S. H., and Wycherley, V., unpublished work). The presence of polyethylene had little influence on the rate of conversion, but in the presence of polyvinyl chloride an extraordinary increase in conversion rates was observed over certain regions of composition.

This encouraged an examination of the products resulting from the irradiation of solid solutions of polyvinyl chloride in diallyl and triallyl esters, when they were found to exhibit the properties associated with a very high density of cross-linking. In Fig. 1, the swelling index (ratio of specimen weight after 24 hr. swelling in tetrahydrofuran at 20° C. to initial weight) is shown for solid solutions of polyvinyl chloride in a diallyl ester (open circles) and in a triallyl ester (solid circles) as a function of radiation dose, in comparison with the swelling index of unplasticized polyvinyl chloride 'Cobex' (square). The enhanced cross-linking of the polyvinyl chloride is further evident from the curves in Fig. 2, showing the tensile strength at 100° C. as a function of radiation dose for solid solutions of polyvinyl chloride in a saturated ester (crosses), in a diallyl ester (half-solid circles), and a triallyl ester (open circles) in comparison with the behaviour of 'Cobex' (solid circles).

A preliminary kinetic analysis of the rates of conversion of the allyl esters as a function of their concentration has indicated the inadequacy of a simple energy-transfer mechanism to explain the results. Coupled with the enhanced density of cross-linking of the polyvinyl chloride, the analysis suggests interaction of the polymer chains, not only with the propagating allyl radicals ($R.\mathrm{CH_2}$—$\dot{\mathrm{C}}\mathrm{H}$—$\mathrm{CH_2O}$—) but also with the resonance-stabilized allylic radicals ($\mathrm{CH_2}$=CH—$\dot{\mathrm{C}}\mathrm{H}$—O—). Reactivation of allylic radicals has been previously proposed to account for increased allyl polymerization rates at very high pressures[5].

The difference in behaviour between polyvinyl chloride and polyethylene may be attributed to the greater ease of abstraction of atoms from the chlorinated polymers, though questions of compatibility of the ester may also be involved. The efficacy of allyl esters probably arises from the short propagation chain-length and the accumulation of stabilized radicals, which renders the action of these monomers quite distinct from that of vinyl monomers, which

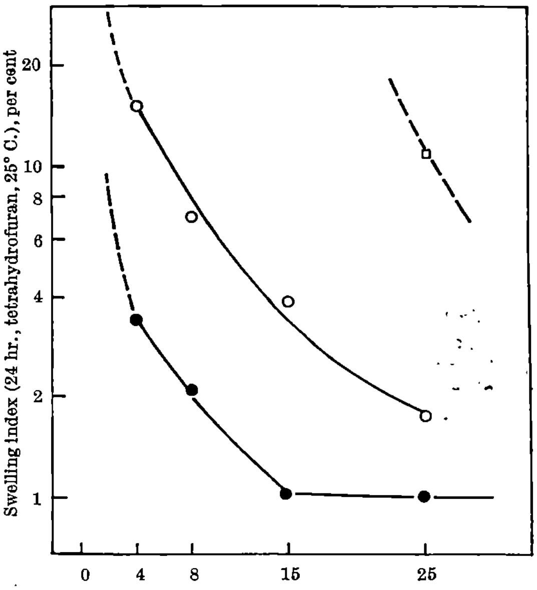

Fig. 1. Swelling of irradiated polyvinyl chloride

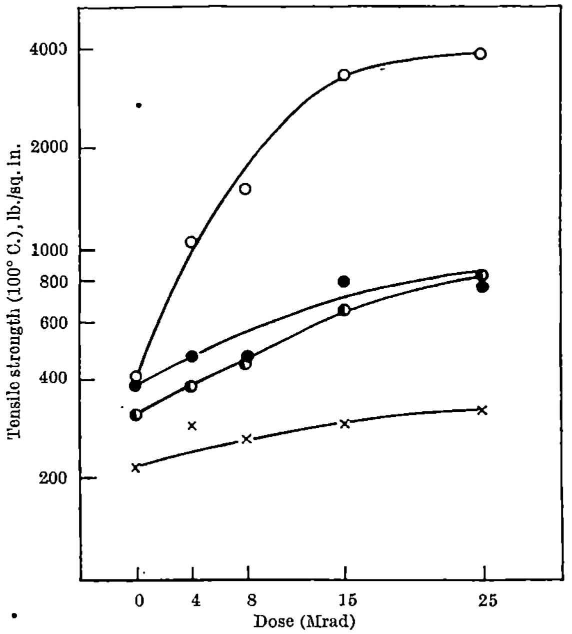

Fig. 2. Tensile strength of irradiated polyvinyl chloride

are also known to be polymerized *in situ* but without comparable involvement with the parent polymer.

Since highly cross-linked vinyl chloride copolymers are thus made readily available through the agency of allyl esters, it seems possible to regard these as 'promotors' for radiation-induced cross-linking, operating by a process of 'secondary initiation' (to distinguish it from primary initiation by the incident radiation) and giving a density of cross-linking much higher than that obtainable by radiation alone.

The kinetic data and theoretical implications of this work will be presented in greater detail in forthcoming publications.

I wish to thank Prof. A. Charlesby for his early interest and encouragement and colleagues at Hinxton Hall for discussions and experimental assistance. Part of this work was carried out in collaboration with B.X. Plastics, Ltd., and I thank the Chairman of B.X. Plastics, Ltd., and the Chairman of Tube Investments, Ltd., for permission to publish this account.

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March 2.

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Adhesion and Ion-Exchange between Mica Surfaces

If the adhesive forces between mica surfaces[1] are due to ionic interactions as has been suggested[2], interchange of ions between two mica surfaces brought into contact might be expected. If matching of ions and sites in the aluminosilicate lattice were complete, we should find a redistribution of the surface ions between the two faces, and if the ion-site forces were the same for any given ion with respect to both sheets, this new configuration should find half the ions from each sheet transferred to the other. Such an exchange has now been found to occur by observing the transfer of radioactive potassium-42 from a mica sheet on to which it had been exchanged from aqueous solution[3] to another sheet initially inactive. When such an experiment was performed by simply pressing the two sheets of mica together on a flat surface, the amount of activity transferred was only 10 per cent of that initially present. This would suggest that the sheets were in contact over only 20 per cent of their area. This result is in line with the initial transfer values for stearic acid monolayers between mica surfaces pressed together, as found by Rideal and Tadayon[4]. When the area of intimate contact was observed by multiple-beam interference techniques, however, the amount of transfer was found to be nearly half the total exchangeable potassium in that area.

Sheets of silvered mica were prepared and used for contact area measurement by the methods described by Bailey and Courtney-Pratt[5]. After cleaving the silvered sheets, and before the pieces were put into contact, the unsilvered side of one piece was rinsed with a 10^{-3} *N* potassium chloride solution containing potassium-42, rinsed with acetone, and dried. The two pieces of mica were then inserted in the clamps and brought into contact under the microscope. The area of uniform tint was measured with a micrometer eyepiece, the strips were then separated (total contact times were 2–8 min.) and the central portion of each, which included the contact area, was cut out and its activity measured under an end-window Geiger–Müller counter. (The area of contact was always a negligible fraction of the total area of the counting sample.) The results are collected in Table 1. Since the mica sheets were not especially selected for thickness, the sensitivity of the contact area measurement was not high nor necessarily reproducible. Especially in the case of the smaller contacts, where the activity transferred was also small, the observed values may be in considerable error. It is apparent, however, that the amount of potassium-42 transferred was very nearly half that initially present on the exchanged sheet. That initial activity, furthermore, was in satisfactory agreement with the activity calculated for complete surface potassium exchange with the solution used (1,300 counts/min./cm.^{2}).

Derjaguin *et al.*[6] have proposed a charge separation mechanism to account for their (rather higher) observed cleavage energies of mica. There seems to be no reason why surface potassium ions distributed in patches might not be invoked to provide their charge mosaic. As they suggest, the forces between such patches would still be large at appreciable separation of the sheets and would lead to gas dis-

Table 1. Observed Potassium-42 Activity on Contacted Mica Sheets

	Exchanged sheet, observed (c./min./cm.^{2})	Contact area (cm.^{2})	Contacted sheet (c./min.) obs.*	Transferred activity (c./min./cm.^{2})
1	1,044	0·052	21·1 (1·9)*	406
2	1,357	0·127	83·2 (3·7)	655
3	1,295	0·011	11·7 (1·6)	1,062
4	879	0·134	31·5 (2·1)	235
	1,144	Average values		590

* Counting standard deviations shown in parentheses. All count-rates corrected for background, counter resolving time, and corrected for decay to the same (zero) time.

charge. At the higher rates of cleavage which they used, moreover, such behaviour may be more likely than if the cleavage occurs as a nearly equilibrium process. (This point has been brought out by Miss Bailey[7].) The present experiments, of course, cannot distinguish between a uniform distribution of potassium ions and an array of small patches, and therefore I am not able to evaluate the importance of this contribution.

I am greatly indebted to Miss C. P. Rutkowski for experimental assistance and to Dr. David Tabor for interesting discussions.

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Feb. 9.

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Material Transfer in Monomolecular Layers of a Boundary Lubricant

Bailey and Courtney-Pratt[1] have studied the shearing of monomolecular layers of calcium stearate between flat mica sheets. They concluded that this shearing in the boundary lubricant film, which may afford almost perfect protection against wear, still contributes significantly to sliding friction. The processes which occur in the contact of such atomically flat surfaces protected by boundary films are therefore of some interest. It has been shown that mica surfaces brought into contact interchange the exchangeable potassium ions on their surfaces (preceding communication). This observation seems to support the postulate that the adhesive force between mica surfaces is ionic in nature[2]. Rideal and Tadayon[3] observed transfer of stearic acid from monolayers deposited on mica to other mica surfaces, but the major portion of their work seems to have been concerned with surface diffusion processes rather than true contact transfer.

In this communication the results of some preliminary measurements of area of true contact and transfer of stearic acid from monolayers, as well as migration of surface potassium ions through such monolayers are reported. The methods of Bailey and Courtney-Pratt[1] were used to measure contact areas and the potassium ion transfer was detected with potassium-42, as in the previous communication. Potassium ion migration was observed from an ion-exchanged mica surface[4] to a sheet of mica coated with a monolayer of commercially pure stearic acid (Armour 'Neo-Fat 18'). Stearic acid transfer was observed by measuring the activity transferred from a mica surface coated with a monolayer of stearic acid labelled with carbon-14 at the carboxyl group to an untreated surface. In both types of experiments, monolayer deposition was accomplished by the Blodgett technique[5], using a distilled water substrate and a surface pressure of about 30 dynes/cm. (oleic acid piston oil). The stearic acid was spread from hexane solution. The results of the transfer measurements are recorded in Table 1.

Table 1. TRANSFER OF POTASSIUM-42 AND STEARIC ACID-^{14}COOH BETWEEN MICA SURFACES

A. Potassium ion transfer in the presence of a stearic acid film

	Potassium-42 exchanged sheet, observed (c./min./cm.^{2})*	Contact area (cm.^{2})	Contacted sheet (c./min.) obs.*	Transferred activity (c./min./cm.^{2})
1	290 (10)	0·052	11·2 (2·8)	214
2	1,100 (15)	0·092	20·6 (1·8)	224
3	900 (10)	0·002	1·7 (1·6)	850

(Samples 2 and 3 from a different lot of potassium-42 than sample 1.)

B. Stearic acid–^{14}COOH transfer.

	Monolayer-coated sheet, observed (c./min./cm.^{2})*†	Contact area (cm.^{2})	Contacted sheet (c./min.) obs.*	Transferred activity (c./min./cm.^{2})
1	313 (3·0)	0·093	6·2 (0·5)	67
2	—	0·0051	1·5 (1·1)	294
3	—	0·016	1·1 (1·0)	68
4	—	0·018	2·0 (1·1)	111

* Counting standard deviations in parentheses. All counting-rates corrected for background, counter resolving-time and decay, where appropriate.

† Samples 1–3 were all coated from the same spread monolayer. Sample 4 was a separate monolayer spread from the same solution.

It is apparent from Table 1 that these results obtained are very crude and must be considered as preliminary. It is, however, clear that some transfer of both stearic acid and potassium ion does occur. Whether transfer of potassium ions occurs here through formation of a soap and migration of the entire soap molecule cannot be decided on the basis of the present results—radioactivity measurements of higher precision (which would require reagents of higher specific activity than were at hand in this work) would be needed to decide this point. The interesting differences in diffusion transfer of monolayers observed by Rideal and Tadayon make this point of some interest in connexion with the processes occurring in boundary lubricant layers. The ability of molecules to move from monolayers on one member of a sliding couple to the other member will be important in the protection of the surfaces, and the possibility of transferring metallic ions either through the monolayer or in conjunction with overturning lubricant molecules must be recognized.

I am indebted to Miss C. P. Rutkowski for assistance with these experiments.

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Feb. 9.

[1] Bailey, A. I., and Courtney-Pratt, J. S., *Proc. Roy. Soc.*, A, **227**, 500 (1955).

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A New Method of Integration Recording

The method now commonly used for recording continuously and in real time the integral of an instrument output signal requires the counting of pips in the final record. It is therefore essentially digital in nature. We have devised in our laboratory an analogue method (patents applied for) that eliminates counting and produces a new form of record, an 'integram', that appears to be particularly interesting and useful for gas chromatography.

The general scheme of the method is shown in Fig. 1. A conventional pen servo responsive to the signal drives the pen across the chart in the usual

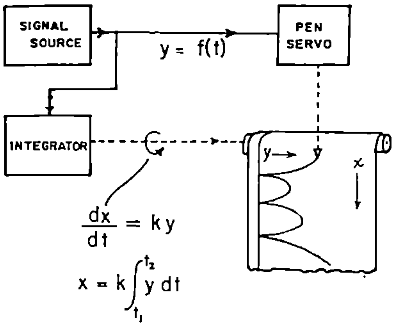
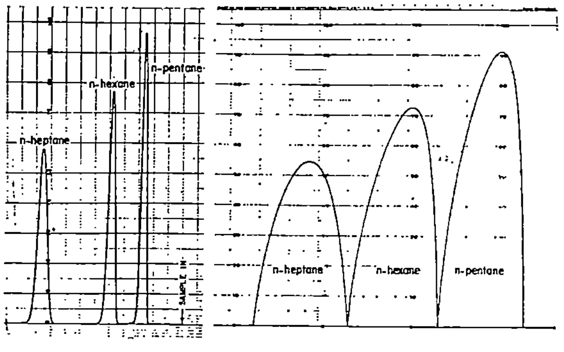


Fig. 1

way. The distinctiveness of the technique lies in the manner of driving the chart, namely, at a rate proportional to the recorded signal. By definition, the required chart drive mechanism is a form of integrator.

The familiar ball-and-disk integrator, with its input shaft driven by the pen transport mechanism and its output coupled to the chart drive, would appear to answer the practical requirements quite well and could be the basis of a relatively low-cost system. In the apparatus we actually employed to make the recordings shown, however, it was expedient to use a velocity servo type of integrator[1]. We inserted a conventional attenuator between the signal source (the gas chromatograph detector) and the pen servo, and a second attenuator (for signal reduction in ratios of 1 : 5 : 20) between the output of the first attenuator and the integrator. The velocity servo comprised a high-gain amplifier driving a motor and a direct-current tachometer. The tachometer output, fed back inversely to the servo-amplifier input, caused the servo output shaft, and thus the chart, to be driven at a rate proportional to the servo input signal.

The separate attenuator at the input of the velocity servo is necessary because the duration of gas chromatography peaks may vary over a considerable range: 20 to 1 or more. Thus, when peaks occur that are long lasting and also of large amplitude, the chart speed per unit of pen deflexion may be reduced to avoid excessive run-off of paper. As an auxiliary paper-saving feature, a switch may be mounted on the recorder whereby the pen drive at the upper limit of travel short-circuits the input to the servo-amplifier. The chart is thereby arrested during intervals when the pen is off the scale. Integration information is, of course, lost during such intervals, but in this respect the system does not differ from other recorder-coupled integrating devices.



(*a*) (*b*)

Fig. 2. (*a*) Chromatogram and (*b*) integram. Sample: 0·02 ml. *n*-pentane, *n*-hexane and *n*-heptane (1 : 1 : 1); chromatogram chart speed, 0·5 in./min.; integram chart speed, 8 in./min./100 per cent signal; column, 6 ft., silicone 550, 40–60 *C*-22 firebrick; temperature, 91° C.

For change-over at any time to conventional chromatographic recording, it is necessary only to operate a switch that substitutes a constant voltage at the input of the servo-amplifier in lieu of the gas chromatographic signal, so that the chart is driven at constant speed.

Fig. 2*b* shows a typical integram. The corresponding conventional chromatogram is shown in Fig. 2*a*. The records shown were run simultaneously on a sample of equal parts of *n*-pentane, *n*-hexane and *n*-heptane. (The discrepancy between corresponding peak heights in the two recordings is due to an inexact divider used at the input of the integram recorder.)

Of primary interest is the property that the base width of each peak in the integram is proportional to the area of the corresponding chromatogram peak.

Thus, the integram shows at once that the components are approximately equal in quantity, a fact not easily discerned in the conventional recording. We note, too, that the integram contours terminate sharply in the base line at well-defined points and with steep slopes, whereas 'skirts' tapering gradually to zero slope appear in the corresponding chromatogram. This has been found to be true even when extensive tailing occurs. The integram therefore clearly defines the integration limits. As a note of interest, the property of sharp termination applies equally to a variety of functions (of signal vs. time) that might be encountered in instrumental measurements, for example, Gaussian distributions, exponential decay and displaced sinusoidal functions such as $y = 1 + \sin \omega t$.

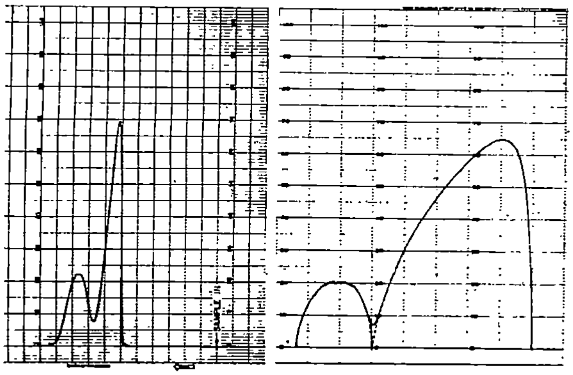


Fig. 3. Incompletely resolved peaks. Sample, 0·03 ml., methyl ethyl ketone and *cyclo*hexane (2 : 1). Conditions as in Fig. 2

Fig. 3 shows an example of the curves obtained on incompletely resolved components. Without prior knowledge of the peak shapes, it would be pure guesswork to extrapolate the overlapping curves in the chromatogram at the left in order to determine individual integration limits. In the corresponding integram, however, extrapolation is much more reliable. Given the degree of resolution shown, we can predict with some confidence (especially for the larger peak) where the extrapolated curves would meet the axis. Experience indicates that the shape of the integram for a given component remains quite characteristic and exhibits no surprising changes of direction as it approaches the axis. Thus a French curve laid against the integram contour can give a useful extrapolation. A point of special interest is that, having extrapolated one of the adjoining, unresolved peaks, we resolve also the uncertainty for the other, because in the integram both extrapolations join the axis at a common point. This follows from the fact that total integram base-width for adjoining peaks is proportional to the sum of the separate integrals and independent of degree of resolution (on the reasonable assumption that detector response is linearly additive for superposed components).

Characteristically, the integram does not indicate elapsed time. Thus the integram of Fig. 2 does not tell how long the signal remained at zero between peaks, or the times at which the maxima occurred. A simple adaptation of the recorder, however, furnishing a supplementary time trace, permits this information to be embodied in the record. The integram may, for example, be confined to half the chart width (without serious loss of accuracy since the quantitative information of interest resides mainly in the width of the integram peaks, not their heights). A second pen is then provided which is driven laterally across the other half of the chart at a suitable constant speed. The supplemental trace thus obtained completely correlates the events of the integram with elapsed time, exhibiting plateaux in the lateral chart direction during the time intervals between peaks, and inflected steps between the plateaux marking the chromatogram peaks.

This work was announced at the Pittsburgh Conference on Analytical Chemistry and Applied Spectroscopy on March 6, 1958.

Allen Strickler
William S. Gallaway

Research and Engineering Department,
Beckman Instruments, Inc.,
Fullerton, California. Jan. 19.

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PHYSICAL SCIENCES

Conductivity induced by Radiation in Polycrystalline Cadmium Sulphide and Polyethylene

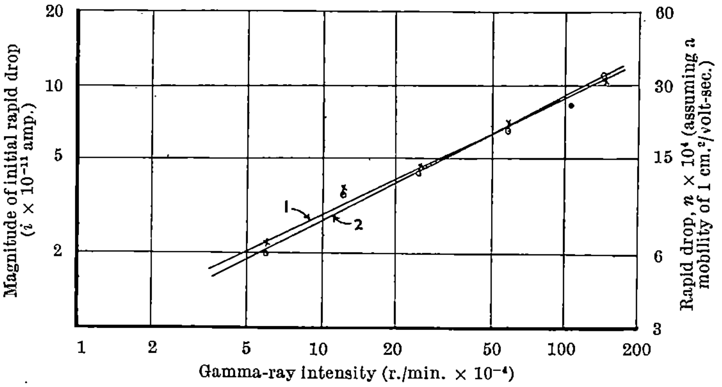

Fig. 1. Two crystals, (1) and (2), of polycrystalline cadmium sulphide at −55° C.

When ionizing radiation falls on insulating or semiconducting solids, there is an increase in electrical conductivity resulting from the production of electron-hole pairs. If the source of ionizing radiation is removed, the conductivity decreases at a rate dependent upon the release of electrons from traps into the conduction band.

For any system with a continuous distribution of traps, it has been shown[1] that the curve of conductivity decay following excitation by radiation is approximately hyperbolic, and is given by the equation:

$$\frac{1}{n} = \frac{1}{n_0} + \frac{(m)}{(M_E)} \frac{bt}{kT} \qquad (1)$$

where n is the number of electrons per unit volume in the conduction band at any time t after removal of the exciting radiation and n_0 is the value of n at $t = 0$; b is the recombination coefficient of electrons with the original centres; m is the number of trapped electrons per unit volume and M_E is the number of traps per unit volume per unit energy-range. The departure from hyperbolic decay in cadmium sulphide has been used by Broser and Broser-Warminsky[2] to calculate the detailed distribution of traps in depth.

This theory leads one to believe that if thermal equilibrium between electrons in the conduction band and those in traps is not valid, as would occur if the rate of release from traps were smaller than the rate of recombination, a rapid drop in current would be observed until the rates became comparable. Thereafter equation 1 would be followed. The time constant for this rapid decay is of the order of $1/bm$. The time constant of the main decay following the rapid fall is of the order of $1/bn_0$; that is, larger than the rapid decay by the ratio m/n, approximately.

We have obtained support for this aspect of the theory from observations of an initial rapid decay in cadmium sulphide and in polyethylene under irradiation by gamma- and X-rays, respectively. Although these substances have conductivities which differ by orders of magnitude, the mechanism of induced conductivity is expected to be the same. Both substances normally show a similar dependence of induced conductivity on dose-rate, namely:

$$\sigma \propto R^{0.85} \qquad (2)$$

where R is the dose-rate.

There are two conditions for which an excess of conduction electrons would be present to cause this initial rapid drop. One is at extremely high intensities of radiation, where the concentration of free carriers, n, would be larger than the concentration of trapped electrons, m; that is, larger than 10^{14}–10^{17} per cm.^{3}. This condition would occur at radiation intensities of the order of megarads per minute. The second condition is found at temperatures sufficiently low to delay significantly the thermal release of electrons from traps, that is, at temperatures below −10° C. in cadmium sulphide, and at room temperature (20° C.) in polyethylene.

Under the conditions described, where an initial rapid drop is observed, the traps are not effective, so that the dependence of steady-state induced conductivity on radiation intensity should follow instead a simple square root relationship:

$$\frac{dn}{dt} = 0 = Q - bn^2$$

$$\text{or,} \qquad n \propto Q^{1/2} \qquad (3)$$

where Q is the ionization-rate per cm.^{3}.

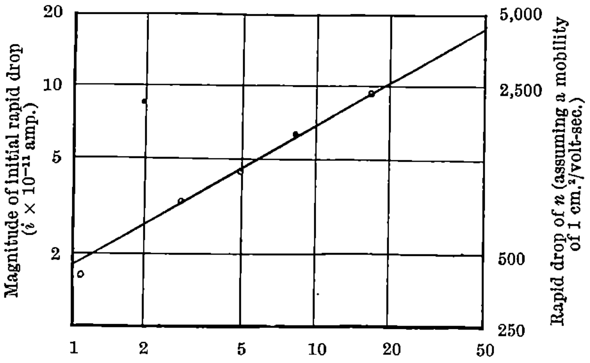

Fig. 2. Polyethylene at + 20° C.

We find experimentally that this is so to a reasonable degree of accuracy.

Fig. 1 shows curves relating to cadmium sulphide in which the logarithm of the magnitude of the initial drop has been plotted against the logarithm of the radiation intensity, yielding an exponent of 0·48 in equation 3. Fig. 2 shows similar curves for polyethylene, where the exponent is 0·56.

For substances with an exponential distribution of traps, Rose[3] gives the variation of induced conductivity with dose-rate and temperature as :

$$\sigma \propto R^{T_1/(T+T_1)} \qquad (4)$$

where T_1 is a constant of the substance which has the dimension of temperature, and which has been suggested as being the 'trap melting point'. Both these substances have values of T_1 about 1,500° K., and it has been shown[2] that for substances having such high values of T_1 an initial drop is more likely than for substances having a lower value of T_1, approaching room temperature.

Support is therefore afforded for the conception of photo-conductive trapping and decay as applied to ionizing radiation falling on insulating or quasi-insulating substances.

We are indebted to Dr. S. T. Henderson, Thorn Electrical Industries, Ltd., for supplying the polycrystalline cadmium sulphide layer cells.

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Refractive Index of Uranium Oxide produced by Anodic Oxidation

During a study of the anodic oxidation of uranium it was found that brilliant interference colours could be obtained using an aqueous solution of ammonia as electrolyte. The film was found to be non-absorbing up to the maximum voltage which could be applied without pitting of the metal, that is, 270 V. Flint *et al.*[1] have studied the anodic oxidation of uranium in various electrolytes and consider that ammoniated ethylene glycol only can be used for producing interference films without pitting.

It was considered that, providing the refractive index could be determined, the kinetics of film growth could be studied with advantage by an optical reflectivity method. Separation of the anodic oxide from the metal was not possible, and the bulk oxide could not be used for this determination since the chemical and physical nature of oxide films produced by anodic oxidation usually differs from oxides prepared thermally or chemically.

An investigation of the solubility of the anodic oxide revealed that it dissolved readily in dilute sulphuric acid, which, however, did not attack the underlying metal. It was thus possible to remove the anodic oxide film completely from part of the specimen, forming a sharp oxide step which could be measured, after silvering, by multiple beam interferometry using reflected light[2]. It is of interest to observe that this method is not applicable to the refractory anodic oxides produced on tantalum, zirconium, niobium and titanium.

The refractive index calculated using this method gave $\mu = 1·93$.

The above technique has, however, been extended to provide a method which is applicable even if the metal is slightly soluble in the acid since, by suitably controlling the dissolution of the oxide in the acid, a wedge of oxide could be produced on the metal surface. An examination of this oxide wedge revealed dark fringes, in the direction of the wedge length, which corresponded to successive orders of interference minima in the oxide. The specimen was suitably mounted in conjunction with a silvered reference flat so that a further fringe system was produced at right angles to the fringe system in the oxide wedge. A composite fringe system was thus obtained in which the multiple-beam fringes became laterally displaced in crossing the wedge. By means of an eyepiece micrometer the intersection of these fringes with the order fringes could be located.

The fringe system is shown diagrammatically in Fig. 1, where *aa* represents order fringes in the oxide wedge and *bb* multiple-beam fringes formed between the flat and specimen. The physical thickness of the oxide between successive interference minima is $\lambda/2\mu$, where μ is the refractive index of the oxide and λ is the wave-length of the light source.

The displacement d of fringe *bb* in passing between adjacent minima *aa* corresponds to an increase in optical path of λ/μ, and the distance D between

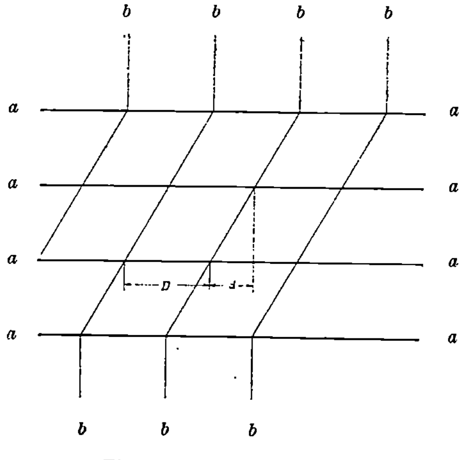

Fig. 1. Composite fringe system

successive *bb* fringes corresponds to change in optical path of λ. Hence,

$$\mu = \frac{D}{d}$$

An average value of several determinations embracing four orders of interference gave $\mu = 1{\cdot}95$ for uranium oxide produced by anodic oxidation.

This value is in good agreement with the value for the refractive index determined by the previous method. The accuracy of the determination was limited by irregularities in the metal surface and by the broad fringes obtained, and it was not possible to determine whether μ varied within the thickness of the oxide wedge.

A determination of the refractive index of thermally prepared uranium oxide by Brewster angle measurements on the polished face of a sintered block gave a much higher value, namely, $\mu = 2{\cdot}26$ for uranium oxide produced thermally.

Using the value $\mu = 1{\cdot}95$, the growth-rate of the oxide during anodizing in ammonia solution was found to be 28 A./V.

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Frequency of Meteorite Falls throughout the Ages

As recently as in 1956 the late Prof. F. A. Paneth, an authority on meteorite investigations, published a paper under the above heading[1], in which he wrote: "iron and stone meteorites did not fall before the late Quaternary".

Thanks to studies carried out here in Sweden on the 'cosmic spherules' discovered by J. Murray in 1876 [2], which are present in the long cores of sediment raised from great ocean depths by the Swedish Deep Sea Expedition in 1947–48 by means of the Kullenberg piston-core sampler[3], we are now able to refute this hypothesis. We have been able to extract from the sediments cosmic spherules identical with those described by Murray but in much greater numbers, from tens to a couple of thousands per kilogram of red clay[4,5]. Also in the deepest sections of cores from the Pacific Ocean, dating back to the Tertiary Age, such spherules were found. It is to be hoped that by more extensive investigations of this kind a new chronology for deep-sea deposits may be evolved, going back much further in time than is possible by means of radioactive measurements.

This communication (detailed papers are being prepared) is chiefly meant to be a plea for studying the cosmic spherules present in long cores of sediment which will be obtained by future deep-sea expeditions. In case the plans for drilling a hole through the deep-ocean sediments down to the underlying bedrock, repeatedly referred to in *Nature*[6], are realized, a study of the cosmic spherules present in the different layers penetrated will afford a unique record of the variations in meteor frequency since the oceans came into existence. This result alone will make it eminently worth while to realize the grandiose project, the total costs of which will amount only to a fraction of the costs of sending a manned rocket to the Moon.

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Chemical Composition of Tektites

In a recent communication, Brian Mason[1] asks that I supply a list of chemical compositions of sedimentary rocks which parallel those of the tektites. I offer the following references for his samples of tektites labelled A_1–G_1. The pages in the following list refer to Pettijohn's book on sedimentary rocks[2]: A_1, 298; B_1, 364; C_1, 319; D_1, 319; E_1, F_1 and G_1, 306. Except for water content, fair agreements between analyses can be secured by selecting analyses from these tables. The low water content of tektites is a real puzzle. There are some small differences in analyses between those listed by Pettijohn and the tektites. It is very probable that some granites of the composition listed by Mason are fused sediments. What would be more interesting than an argument about average sedimentary rocks would be a comparison of the composition of particular groups of tektites and sedimentary or igneous rocks in the general area in which the tektites are found. If cometary collisions melted the local rock and scattered the fragments over great distances[3], it should be possible to find the original material at an appropriate place. But this requires study by an expert in these matters and probably additional observational data, and these cannot be supplied by me.

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BIOCHEMISTRY

Are Nucleoside Triphosphates Precursors of Mammalian Ribonucleic Acid *in vivo*?

When albino rats are kept for 6–7 weeks on a protein-free diet they lose about half their body-weight[1]. At the same time, almost 50 per cent of the liver proteins and ribonucleic acid disappear: this can only be explained by a decrease in their biosynthesis.

We have studied the liver supernatant, because in this particular fraction loss of nucleoside di- and tri-phosphates during differential centrifugation can be prevented by the addition of ethylenediamine tetraacetate to the separation medium, whereas nucleoside polyphosphates are hydrolysed to monophosphates in the mitochondria and microsomes.

Protein deprivation results in the disappearance of 56 per cent of the proteins and 36 per cent of the ribonucleic acid in the supernatant, while there is an accumulation of adenosine triphosphate (4·7 times the control), guanosine and uridine triphosphates.

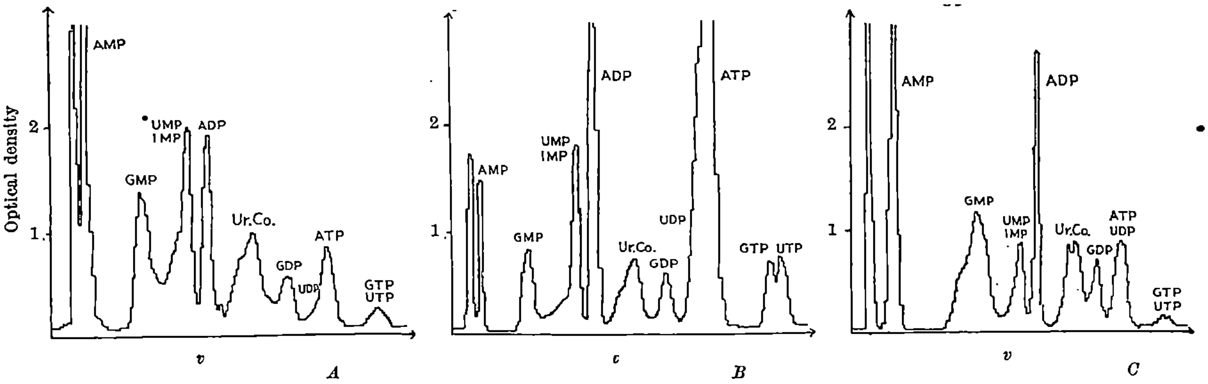

Fig. 1. Free nucleotides of rat liver supernatant, separated on a column of 'Dowex' 1×8, 200–400 mesh, 0·8 cm. × 30 cm. Gradient elution through formic acid and formic acid – ammonium formate: *A*, controls; *B*, deprived animals; *C*, protein deprivation followed by normal feeding

Note the increased ATP, GTP and UTP (adenosine, guanosine and uridine triphosphates) peaks after protein deprivation, and the return to normal when rats are fed normally for three days after six weeks protein deprivation.
Optical density measured at 2600 A. in a 1-cm. cuvette; *v*, eluant volume; *Ur.Co*, uridine coenzymes

No cytosine triphosphate could be detected in our experimental conditions either in controls or in deprived animals. This increase of nucleoside triphosphates, parallel with the reduction in the synthesis of ribonucleic acid, suggests that these nucleotides are the precursors of ribonucleic acid. The decrease of ribonucleic acid in the supernatant cannot be due to absence from the diet of the amino-acids glycine, glutamic acid and aspartic acid, precursors of the purine and pyrimidine rings, since these amino-acids are not indispensable.

The results show, for the first time in the case of mammals *in vivo*, that the synthesis of ribonucleic acid is dependent on the synthesis of protein: after protein deprivation, we find a drop in proteins and in ribonucleic acid but an accumulation of nucleoside triphosphates in the supernatant; when rats, deprived of proteins for six weeks, are afterwards fed normally for three days, a rapid increase in proteins occurs, which is paralleled by that of ribonucleic acid, while the nucleoside triphosphates revert to normal levels.

We also incubated whole liver slices of controls and deprived animals for 20 min. at 37° C. with or without a complete mixture of amino-acids. These amino-acids are without effect on the incorporation of phosphorus-32 into ribonucleic acid in the controls. In the case of deprived animals, in which the pool of free amino-acids is certainly small, incorporation of phosphorus-32 is considerably enhanced by the addition of the amino-acid mixture. This suggests that the syntheses of protein and of ribonucleic acid are concurrent processes (which we are now trying to prove by the use of amino-acids labelled with carbon-14). No net increase in the quantity of ribonucleic acid can be detected in such a brief time of incubation, but the greater incorporation of phosphorus-32 seems to afford sufficient evidence. The fact that the ribonucleic acid fraction remaining after protein deprivation shows a greater incorporation (*in vivo* as well as *in vitro*) is discussed elsewhere[2].

Table 1. INCORPORATION OF PHOSPHORUS-32 INTO RAT LIVER RIBONUCLEIC ACID *in vitro*

Whole liver slices were incubated for 20 min. at 37° C. with or without a complete mixture of amino-acids. Values are in c.p.m. per 100 μgm. of ribonucleic acid phosphorus

Experiment No.		Without amino-acids	With amino-acids
1	Controls Deprived animals	490 2,610	570 4,550
2	Controls Deprived animals	400 2,060	520 3,560

In other words, while it appears to be well established that ribonucleic acid is indispensable in protein synthesis, it also seems that little or no ribonucleic acid is synthesized when protein synthesis is stopped or at least slowed down by deprivation of nitrogen. This agrees with facts observed in micro-organisms[3]. In any event, it seems highly improbable in the light of present knowledge that the cell should synthesize proteins on one hand and ribonucleic acid on the other, both of which would afterwards combine to form specific nucleoproteins. The synthesis not of proteins and ribonucleic acid separately but of nucleoproteins from amino-acids and nucleotides would explain the known facts, namely, the role of ribonucleic acid in protein synthesis and vice versa. This synthesis of ribonucleoproteins may occur by condensation of nucleotide – amino-acids complexes. Hitherto, only adenosine monophosphate–acyl complexes have been described. Our hypothesis postulates the existence of guanosine, uridine and cytosine monophosphate complexes. The fact that these complexes have not so far been discovered does not constitute proof that they do not exist.

This hypothesis might be extended to other classes of heteroproteins. Hendler[4] recently reported that lipids play a part in the synthesis of proteins. It is possible that synthesis of certain lipoproteins occurs through condensation of amino-acid – lipid complexes, and that of some glycoproteins by condensation of amino-acid – saccharide complexes.

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Stizolobic Acid : a New Amino-Acid in *Stizolobium hassjoo*

Two new amino-acids have been found in the sap exuded from the cut surface of the epicotyl tips of etiolated seedlings of *Stizolobium hassjoo*, all parts of which turn black on dying owing to the oxidation of 3,4-dihydroxyphenylalanine. The exudate contains 3,4-dihydroxyphenylalanine and two new amino-acids, as shown by paper chromatography. The R_F values of the latter amino-acids coincided with no amino-acids already known, and it is proposed that these compounds be named stizolobic acid and stizolobinic acid, respectively. Stizolobic acid gives rise to an orange spot with ninhydrin ($R_F = 0 \cdot 16$ in phenol/water (8 : 2 w/w), 0·11 in *n*-butanol/acetic acid/water (4 : 1 : 2 v/v)), while stizolobinic acid gives a brown spot ($R_F = 0 \cdot 24$ in phenol/water, 0·14 in *n*-butanol/acetic acid/water).

Stizolobic acid was isolated from the combined exudates by ion-exchange column chromatography (*IR*–4*B*—0·05 *N* hydrochloric acid displacement) and obtained as colourless needles, which melted at 231–233° C. after recrystallization. Since the content of stizolobic acid in the plant is very small, the yield from about 10 kgm. seeds was only 10 mgm.

The empirical formula of stizolobic acid was found to be $C_9H_9O_6N$ (found: C, 47·91; H, 3·96; N, 6·45 per cent; calc.: C, 47·62; H, 4·00; N, 6·17 per cent). All nitrogen belongs to amino group as measured by van Slyke's method (found amino-nitrogen, 6·05 per cent). It was shown to contain an α-amino group by its complexing with copper[1], and to be an acidic amino-acid by paper electrophoresis. The results of alkaline titration of the carboxyl group in 90 per cent ethanol showed that it was possibly a dibasic acid. Addition of bromine was not successful, and attempted reaction with carbonyl reagents was also unsuccessful. However, stizolobic acid was attacked by ozonolysis and absorbed about 2·5 mol. hydrogen on catalytic hydrogenation in the presence of a palladium–carbon catalyst, yielding two products, both of which were acidic amino-acids and gave purple spots with ninhydrin. One of them, which was a major product when hydrogenation was interrupted soon after 2 mol. per cent had been absorbed, reacted with 2,4-dinitrophenylhydrazine to form yellow crystals. These properties made it probable that stizolobic acid itself might have a special type of carbonyl group or groups and two —C=C— bonds, and led us to suppose the presence of a γ-pyrone nucleus.

Many γ-pyrone compounds absorb 2–3 mol. hydrogen on catalytic hydrogenation, producing tetrahydro-γ-pyrone compounds and tetrahydro-γ-pyranol compounds, the former reacting with carbonyl reagents[2]. If a γ-pyrone is assumed to be present as an integral part of stizolobic acid, it would readily explain the fact that the carbonyl group does not show ordinary addition reactions, and suggest that the two products are probably a tetrahydro-γ-pyrone compound and tetrahydro-γ-pyranol compound.

The analysis of infra-red spectra of stizolobic acid and its deuterated product gave further support for the γ-pyrone structure of stizolobic acid (Fig. 1). From the data, considering chemical properties, the presence of the following groups could be deduced: NH_3^+, COO^-, non-ionized COOH group (another carboxyl group), two or more H atoms in $=\overset{\mathrm{H}}{\overset{|}{\mathrm{C}}}-$ groups and one or more —C=C— groups probably conjugated with a —C=O group. The spectra are also not inconsistent with the presence of a =C—O—C= group.

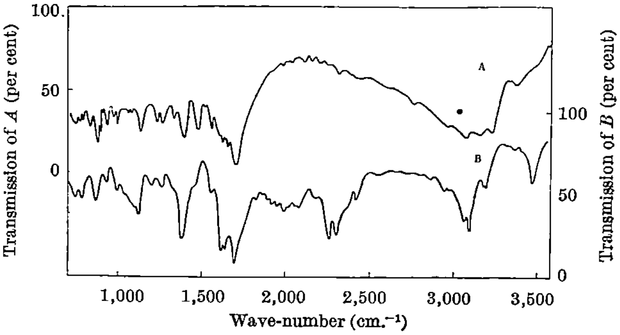


Fig. 1. *A*, Infra-red spectrum of stizolobic acid. Solvent: hexachlorobutadiene (1,300–1,500 cm.$^{-1}$); *B*, infra-red spectrum of its deuterated product. Potassium bromide disk (750–1,800 cm.$^{-1}$). Solvent: hexachlorobutadiene (1,800–3,500 cm.$^{-1}$)

Ozonolysis of stizolobic acid gave aspartic acid, oxalic acid and formic acid. Aspartic acid was also produced on oxidation with potassium permanganate. From these results it seemed likely that stizolobic acid might contain $=CCH_2CH(NH_2)COOH$, $=CCOOH$ and $=CH$ groups. Considering the possible presence of the γ-pyrone nucleus, the structure of stizolobic acid might be assumed to be β-(carboxy-γ-pyronyl)-alanine.

Degradation with boiling 3*N* sodium hydroxide for 3 hr. gave glutamic acid as a major ninhydrin-reacting product and malonic acid, oxalic acid and another unidentified acid as non-volatile organic acids, and formic acid. No acetone was detected. From the examples of alkaline degradation of chelidonic acid[3], comanic acid[4], 2,6-dimethyl-γ-pyrone-3,5-dicarboxylic acid[5] and other γ-pyrone compounds[2,6], formation of glutamic acid by the alkaline degradation of stizolobic acid indicates that the side-chain $—CH_2CH(NH_2)COOH$ might be not on the C_2- or C_6-position, but on the C_3- or C_5-position. Formation of formic acid suggests that there might be no substituent on the C_2- and/or C_6-position, and since malonic acid is produced, the position of the carboxyl side-chain could not be deduced to be attached to other than the C_3- or C_5-position.

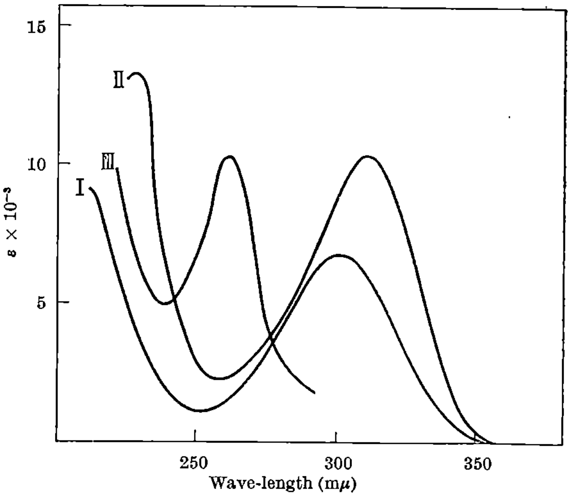
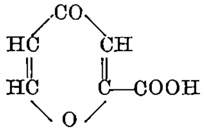
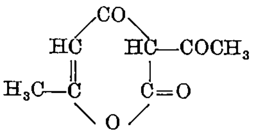


Fig. 2. Ultra-violet spectra of I, stizolobic acid; II, dihydro-acetic acid; III, comanic acid

Some evidence of the position of the carboxyl side-chain is provided by the ultra-violet spectrum. Assuming that stizolobic acid has a carboxyl group as side-chain on the C_2- or C_6-position of the γ-pyrone nucleus, its ultra-violet spectrum might be similar to that of comanic acid (I). However, the spectrum of the former ($\lambda_{max.} = 300$ mμ) differs from that of the latter ($\lambda_{max.} = 260$ mμ), but is similar to that of dehydroacetic acid (II, $\lambda_{max.} = 310$ mμ), which exists as a virtually completely enolized species in solution[7] (Fig. 2). As this form (II*a*) is similar from the point of view of ultra-violet absorption to the postulated structure of stizolobic acid (III), excepting that there is a —OH group on the C_2-position in (II*a*), which would be expected to shift the maximum of the spectrum by 10–20 mμ to longer wave-length, the postulated structure of stizolobic acid is not inconsistent with ultra-violet absorption data.


(I)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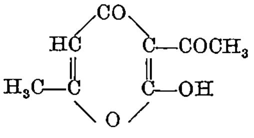
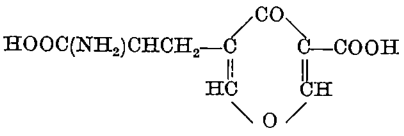

(II*a*)


(III)

The results of electrophoresis indicated that stizolobic acid is a considerably stronger acid than other monoamino-dicarboxylic acids such as aspartic acid. This finding confirms the assumption that the side-chain of a carboxyl group might be on either the C_3- or C_5-position in the γ-pyrone nucleus, both of which would be expected to enhance the acidity, while a carboxyl group on the C_2- or C_6-position would be expected to show a weak acidity, because of a proton-attractive —O— group.

From all the evidence described above, it appears that stizolobic acid has the structure β-(3-carboxy-γ-pyron-5-yl)-alanine. In recent years a number of new, unusual amino-acids have been isolated from plant materials; but an amino-acid with a γ-pyrone nucleus such as stizolobic acid has not been found hitherto. It has been shown to be present in the various organs of *Stizolobium deeringianum, S. hassjoo, S. pruriens, S. utilis* and *Mucuna irukanda,* but it could not be detected in seeds of *Arachis hypogaea, Azukia angularis, Canavania gladiata* var. *alba, Glycine max, Phaseolus vulgaris, Pisum sativum, Vicia faba, Vigna sinensis* or *Wistaria floribunda,* or in the hydrolysate of the protein prepared from seeds of *Stizolobium hassjoo.*

A fuller account of the investigation will be published elsewhere.

Our thanks are due to Dr. E. C. Bate-Smith, of the Low Temperature Research Station, Cambridge, for revising the manuscript.

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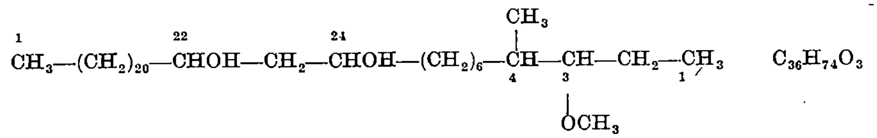
Structure of Phthiocerol

PHTHIOCEROL, a characteristic constituent of the waxes of human and bovine strains of tubercle bacilli[1–3], was found by Stodola and Anderson[1] in 1936 to be a methoxy-glycol with the formula $C_{34}H_{67}(OH)_2OCH_3$ or $C_{35}H_{69}(OH)_2OCH_3$. About ten years ago it was shown that phthiocerol has a long-chain structure with a methyl branch in position 4[4–6]. More recently the presence of a β-glycol grouping was demonstrated[7,8], and several structural formulæ have been suggested on the basis of degradation experiments (for a review see ref. 9). Definite evidence that the methoxyl group is attached to carbon atom 3 adjacent to the methyl group was first obtained by a mass spectrometric study of phthiocerol[10,11], and this was afterwards confirmed by chemical studies[12–14]. The mass-spectrometric results also indicated the presence of a hydroxyl group in position 22 from the straight-chain end of the molecule. The mass spectrum of a purified sample of phthiocerane, the hydrocarbon obtained by reduction of phthiocerol[15], showed this compound to consist mainly of 4-methyltetratriacontane[11]. Structure (I) for phthiocerol was suggested on the basis of the mass spectrometric study[11].

However, oxidative degradation of phthiocerol was found to give two acids, considered to be *n*-tetracosanoic acid[7,16] and a C_{11}-methoxy-acid respectively[16,17]. These results, together with the previously available evidence, led Drayson *et al.*[14] to put forward formula (II) for phthiocerol. Previously one of us (H. D-G.)[12] had suggested that phthiocerol was a mixture of (I) and (II).

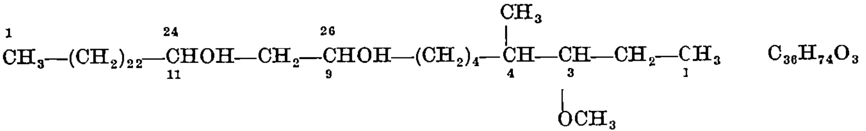
Formula (II) takes no account of the fact that the 'tetracosanoic acid' obtained by chromic acid oxidation of phthiocerol following the procedure of Polgar *et al.* has been shown[11] to be a mixture of the normal chain carboxylic acids with 24, 23, 22 and 21 carbon atoms. The molar relations between these acids were 51 : 9 : 38 : 2. As it seems unlikely that the C_{22} and C_{21} acids have been formed by secondary processes from the C_{24} acid initially formed, the results appear explainable only on the assumption that phthiocerol from natural sources is a mixture of two glycols. One of these glycols must have the first hydroxyl group in position 22 from the straight-chain end and the other the same group in position 24.

In order to clear up this matter, the products of the oxidative degradation of phthiocerol have been examined in some detail. The acidic products formed on oxidation using the procedure described by Drayson *et al.*[14] were converted into methyl esters by means of diazomethane and analysed by gas chromatography and mass spectrometry. The methyl ester of the 'tetracosanoic acid' fraction from a specimen of phthiocerol obtained from Dr. Polgar was found



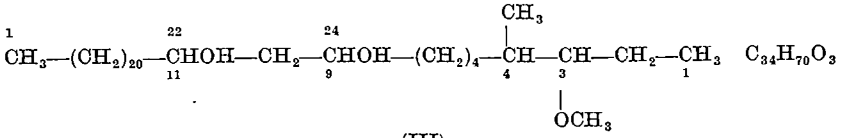
$$\overset{1}{\mathrm{CH_3}}\text{—}(\mathrm{CH_2})_{20}\text{—}\overset{22}{\mathrm{CHOH}}\text{—}\mathrm{CH_2}\text{—}\overset{24}{\mathrm{CHOH}}\text{—}(\mathrm{CH_2})_6\text{—}\underset{4}{\overset{\mathrm{CH_3}}{\mathrm{CH}}}\text{—}\underset{\mathrm{OCH_3}}{\underset{3}{\mathrm{CH}}}\text{—}\mathrm{CH_2}\text{—}\underset{1}{\mathrm{CH_3}}\qquad \mathrm{C_{36}H_{74}O_3}$$

(I)



$$\overset{1}{\mathrm{CH_3}}\text{—}(\mathrm{CH_2})_{22}\text{—}\underset{11}{\overset{24}{\mathrm{CHOH}}}\text{—}\mathrm{CH_2}\text{—}\underset{9}{\overset{26}{\mathrm{CHOH}}}\text{—}(\mathrm{CH_2})_4\text{—}\underset{4}{\overset{\mathrm{CH_3}}{\mathrm{CH}}}\text{—}\underset{\mathrm{OCH_3}}{\underset{3}{\mathrm{CH}}}\text{—}\mathrm{CH_2}\text{—}\underset{1}{\mathrm{CH_3}}\qquad \mathrm{C_{36}H_{74}O_3}$$

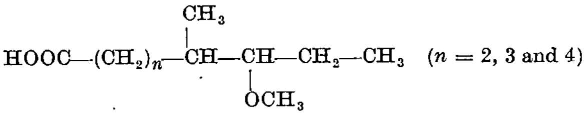
(II)



$$\overset{1}{\mathrm{CH_3}}\text{—}(\mathrm{CH_2})_{20}\text{—}\underset{11}{\overset{22}{\mathrm{CHOH}}}\text{—}\mathrm{CH_2}\text{—}\underset{9}{\overset{24}{\mathrm{CHOH}}}\text{—}(\mathrm{CH_2})_4\text{—}\underset{4}{\overset{\mathrm{CH_3}}{\mathrm{CH}}}\text{—}\underset{\mathrm{OCH_3}}{\underset{3}{\mathrm{CH}}}\text{—}\mathrm{CH_2}\text{—}\underset{1}{\mathrm{CH_3}}\qquad \mathrm{C_{34}H_{70}O_3}$$

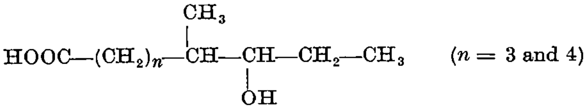
(III)

to consist of a mixture of the methyl esters of the C_{24} to C_{20} acids in the ratios 42 : 18 : 28 : 10 : 1, when subjected to gas chromatography at a temperature of 245° using silicone as stationary phase. Gas chromatography of the 'C_{11}-methoxy'-fraction on 'Apiezon *L*' at a temperature of 199° gave five fractions, which on mass spectrometric analysis were found to be methyl esters of three methoxy-acids:



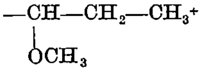
$$\mathrm{HOOC}\text{—}(\mathrm{CH_2})_n\text{—}\overset{\mathrm{CH_3}}{\mathrm{CH}}\text{—}\underset{\mathrm{OCH_3}}{\mathrm{CH}}\text{—}\mathrm{CH_2}\text{—}\mathrm{CH_3}\quad (n = 2,\ 3 \text{ and } 4)$$

and two hydroxy-acids:



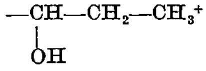
$$\mathrm{HOOC}\text{—}(\mathrm{CH_2})_n\text{—}\overset{\mathrm{CH_3}}{\mathrm{CH}}\text{—}\underset{\mathrm{OH}}{\mathrm{CH}}\text{—}\mathrm{CH_2}\text{—}\mathrm{CH_3}\quad (n = 3 \text{ and } 4)$$

The mass spectra provide highly specific information in this case. The methoxy-esters give an intense peak at $m/e = 73$, which is also found for phthiocerol[11]. This peak is due to the ionized fragment:



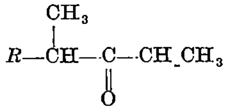
$$\text{—}\underset{\mathrm{OCH_3}}{\mathrm{CH}}\text{—}\mathrm{CH_2}\text{—}\mathrm{CH_3}^+$$

formed by cleavage of the chain between the carbon atoms carrying the methyl and the methoxyl group respectively. The hydroxy-esters just referred to, as well as the triol[7] obtained by demethylation of phthiocerol, give the analogous ion:



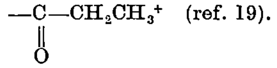
$$\text{—}\underset{\mathrm{OH}}{\mathrm{CH}}\text{—}\mathrm{CH_2}\text{—}\mathrm{CH_3}^+$$

of $m/e = 59$ (ref. 19), whereas oxo-compounds of the general structure:



$$R\text{—}\overset{\mathrm{CH_3}}{\mathrm{CH}}\text{—}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\text{—}\mathrm{CH_2CH_3}$$

give a corresponding large peak at $m/e = 57$ due to the ion:



$$\text{—}\underset{\mathrm{O}}{\underset{\|}{\mathrm{C}}}\text{—}\mathrm{CH_2CH_3}^+\quad \text{(ref. 19).}$$

Quantitatively, the largest components of the 'C_{11}-methoxy'-fraction were the methyl ester of the C_{11}-methoxy-acid (about two-thirds of the total) and the methyl ester of the C_{10}-methoxy-acid, confirming the conclusions of Drayson *et al.*[14] that phthiocerol has a hydroxyl group in position 9 from the branched chain end. The ratio between the C_{11} and the C_{10}-methoxy-acids was about the same (3 : 1) as between the $C_{24} : C_{23}$ and $C_{22} : C_{21}$ pairs of acids respectively derived from the other end of the molecule. This evidence is in agreement with the view that phthiocerol is a mixture of two glycols. The compound might be either a mixture of two homologous β-glycols or a mixture of a β- and a δ-glycol[9,12].

In order to distinguish between these two possibilities, we have examined a specimen of phthiocerane[15] which we had prepared without recourse to purification by repeated crystallization from solvents. Gas chromatography on silicone at a temperature of 265° afforded a clean separation of this material into two fractions, the retention times being 13·8 and 22·2 min. respectively. A specimen of synthetic 4-methyltetratriacontane was found to have a retention time of 22·3 min. under the same conditions, and mass spectrometric examination of the isolated fractions from phthiocerane showed them to consist of 4-methyldotriacontane ($C_{33}H_{68}$) and 4-methyltetratriacontane ($C_{35}H_{72}$) respectively.

The results now reported show that phthiocerol is a mixture of two homologous β-glycols (II) and (III) with 36 and 34 carbon atoms respectively.

The quantitative relation between the C_{35} and the C_{33} components of phthiocerane (from B.C.G.) were approximately the same (3 : 2) as the ratio between the C_{24} and the C_{22} acids obtained by oxidation of a specimen of phthiocerol derived from virulent strains. As the specimens of phthiocerol had all been purified by crystallization from solvents, it seems likely that the homologues (II) and (III) are present in about equal proportions in the bacterial lipids.

The possibility that phthiocerane was a mixture of 4-methyldotriacontane and 4-methyltetratriacontane was suggested previously[5], but considered unlikely at that time because of the reported failure to separate phthiocerane into components by molecular distillation[15].

We are indebted to Prof. R. J. Anderson, Yale University, for specimens of phthiocerol and phthiocerane, and to Dr. N. Polgar, Oxford, for specimens of phthiocerol and of C_{11}-methoxy-acids.

We also thank the Fondation Waksman pour le Développement des Recherches microbiologiques en France and the Swedish Medical Research Council for several grants, and Drs. J. Tréfouël and J. Bretey

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Detailed accounts of this work will be published elsewhere.

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Changes produced in Serum Lipoproteins of Dogs by Cellulose containing Methyl Groups

It has been observed by several authors that macromolecular polysaccharides, especially those containing sulphate groups, cause significant alterations in the lipoprotein patterns of sera[1,2]. In the course of previous studies on the effect of methylcellulose on blood-proteins[3] certain changes in serum lipids were also noted. So it seemed to be of interest to examine what influence methylcellulose of high molecular weight (82,000) exerts *in vitro* as well as *in vivo* on the lipoproteins of sera of experimental animals.

Paper electrophoretic patterns of the lipoproteins in dog and rat sera were obtained after adding solutions of methylcellulose (in concentrations varying progressively from 1·5 to 0·1 per cent). Fig. 1 shows that the presence of methylcellulose considerably alters the chylomicrons but no change can be seen in the α- and β-lipoprotein fractions. The extent of the chylomicron zone is about the half that on the control strip and it is characterized by a sharp peak towards the line of application. The intensity of this peak tends to increase with the concentration of methylcellulose in the serum. Just the same change appeared in the lipoprotein pattern of sera of dogs 30–60 min. after they had received an intravenous injection of a 1 per cent solution of methylcellulose, but disappeared again in a short time. If a solution of methylcellulose was layered over lipæmic sera in capillary tubes, a loose aggregate was formed which later moved slowly upward, while the opalescence of the serum below the interface cleared up. These results suggest that methylcellulose is capable of exerting considerable influence on the large lipid particles of sera.

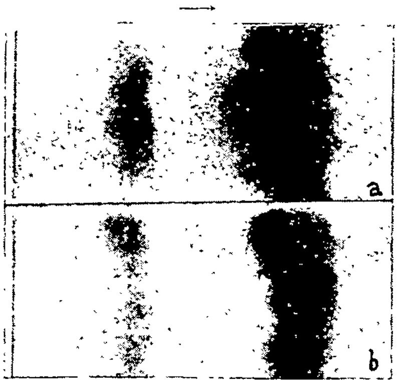

Fig. 1. (*a*) Lipoprotein electrophoretogram of normal dog serum; (*b*) the same serum after the addition of methylcellulose solution

The lipoprotein pattern of dogs treated with 20 ml. of a 1 per cent solution of methylcellulose administered intravenously twice weekly for 3–5 months is presented in Fig. 2. The remarkable increase of a component between the alpha and beta peaks—faintly visible in some of the normal cases—can be observed on the electrophoretogram of dogs treated with methylcellulose. Furthermore, a significant rise in the cholesterol-level was also found after long-term treatment, its mean value being 340 mgm. per cent in treated and 222 mgm. per cent in untreated animals, respectively. Thus long-term administration of methylcellulose alters not only the electrophoretic pattern of lipoproteins but the cholesterol content of blood as well.

Results obtained by paper-electrophoresis with rats injected intraperitoneally with methylcellulose, as well as those described above, do not show any similarity to the heparin-like effect of cellulose sulphate described by Constantinides[1]. It seems therefore that the substituent groups are an important factor in the mode of action of macromolecular polysaccharides on the lipoproteins. Not only the character of the changes caused but also the

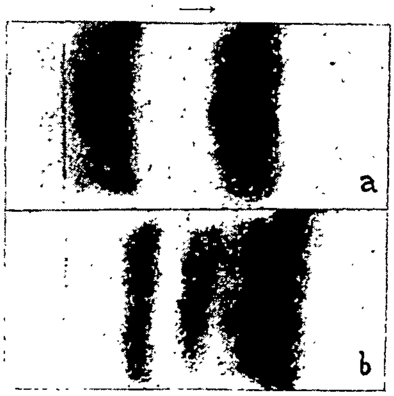

Fig. 2. Lipoprotein electrophoretogram of dog serum, (*a*) before, and (*b*) after, methylcellulose treatment

time needed for their establishment depends on the substituents.

Histological examination of six dogs after long-term treatment showed infiltrations mostly containing mononuclear cells in the wall of the small arteries, perivasculitis, a considerable intima proliferation and formation of granuloma in the interstitium of the lung tissue. This histological picture resembles that of thromboembolic arteriitis.

Further experiments are in progress in order to elucidate the mode of action of methylcellulose on the lipoproteins, as well as the relation between the lipoprotein disturbances and the histological picture.

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Gas-Chromatographic Observation of the Reduction of Carbon Dioxide to Methane during Anaerobic Digestion

Gas chromatography has been applied to the analysis of gases formed during methane fermentations[1]. It appeared to us that this technique could be used successfully for observing the mechanism of methane formation. Knowledge of the biochemistry of methane-producing bacteria is still superficial in many respects. Early observations of Söhngen[2] showed the possibility of the fermentation of a mixture of carbon dioxide and hydrogen by enrichment cultures of some anaerobic bacteria. These micro-organisms could couple the oxidation of hydrogen with the reduction of carbon dioxide to methane. More recently, Barker[3] had discussed the mechanisms by which carbon dioxide could be the precursor of methane.

In this laboratory a method of analysis of fermentation gases was applied using gas chromatography to separate various components of the gas mixture by argon elution from an absorption column packed with activated carbon. The detection of these components was achieved by a beta-radiation ionization chamber (ref. 4 and personal communication from A. T. James). A method based on this principle allowed the determination during a single analytical procedure of hydrogen, nitrogen, methane and carbon dioxide.

The gas-chromatography apparatus consisted of the sample-injection system, manometer, chromatographic column in an electrically heated jacket, beta-radiation detector, soap-film flowmeter and carrier-argon supply cylinder. The source of β-rays for the ionization chamber detector was 10 mc. of strontium-90 in silver foil in the shape of an open cylinder, which was mechanically and electrically joined to the body of the chamber. The chamber itself was constructed of brass and a 'Champion' *C*–5 sparking plug, modified by the addition of a brass cap, was used as the central collecting electrode, with the radioactive cylinder surrounding it. The gas inside the cell of the detector was bombarded with β-particles and was ionized. When the walls of the chamber (and the radioactive electrode) were connected to a source of 300 V. from a voltage stabilizer, the ionization current collected by the central electrode was amplified and recorded by a Honeywell–

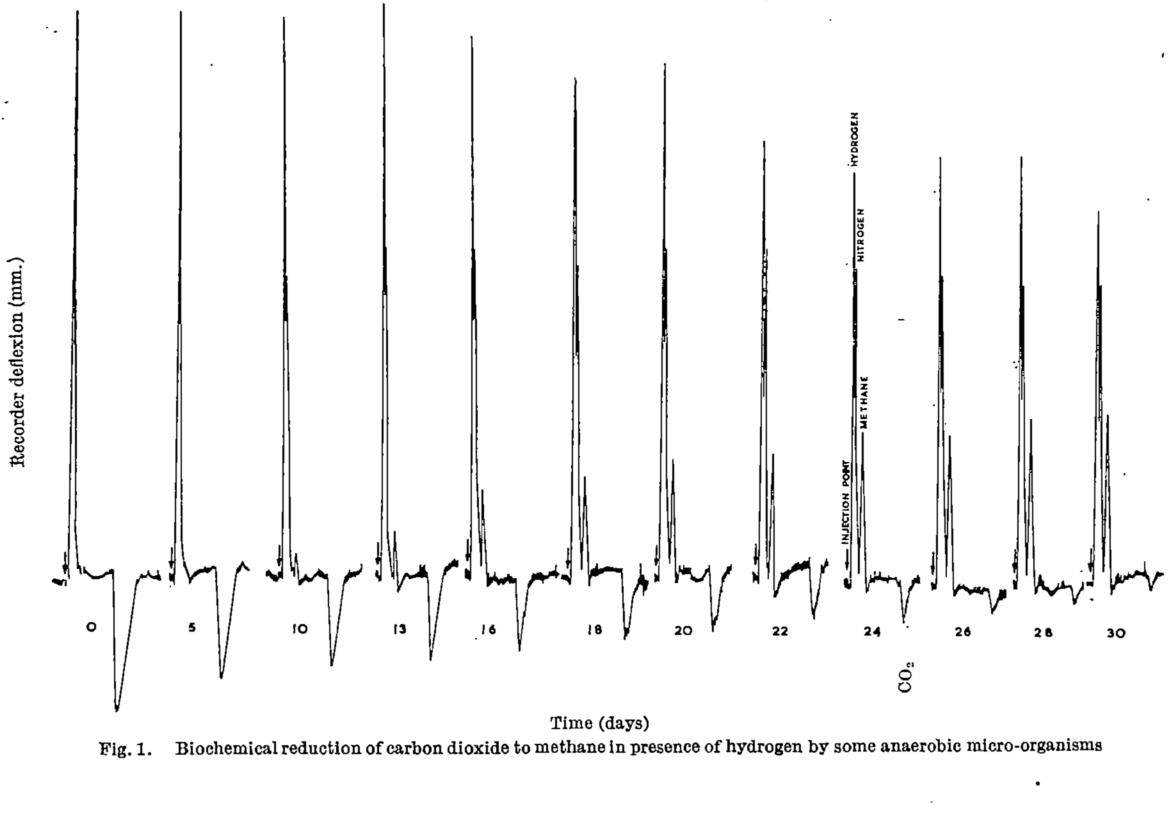

Fig. 1. Biochemical reduction of carbon dioxide to methane in presence of hydrogen by some anaerobic micro-organisms

Brown potentiometric recorder. The amplifier was adjusted so that the recorder indicated the chosen base-line for the constant flow of pure argon, and gave a deflexion for argon carrying other gases. The gaseous constituents separated by the chromatographic column were detected and recorded as more or less separate peaks on the time-deflexion graphs of the recorder. Relationships between peak height and volume of gas sample for hydrogen, nitrogen, methane and carbon dioxide were established and used as calibration curves for the determination of the gases resulting from the anaerobic processes. Higher sensitivity of the ionization detector for hydrogen and nitrogen than for carbon compounds was observed in this investigation. All the determinations were performed under standardized conditions as indicated in the next paragraph.

The chromatographic column used was a glass tube, of approximately 4 mm. diameter and 4 ft. long, packed with about 6·5 gm. of activated carbon (Sutcliffe, Speakman No. *B*–206) ground to 30–70 mesh. Both the chromatographic column and the ionization chamber were enclosed in a heating jacket with temperature-control equipment which maintained the temperature at 50 ± 0·5° C. to ensure the stability of the chromatographic sorption processes. The rate of flow of the carrier argon has been fixed at 46 ml./min., which required an input pressure of 230 mm. mercury. Samples of 5 or 10 ml. of gas under investigation were measured under atmospheric pressure by hypodermic syringe and were introduced to the flow of carrier argon through a rubber serum cap on the top of the column.

Some preliminary observations have been made of the biochemical reduction of carbon dioxide to methane during anaerobic fermentation. Volumes of 2·5 l. of fully digested sewage sludge were placed in 10-l. reacting bottles supported with their axes horizontal on rubber-covered rollers. These reactors were fitted with 'Perspex' stationary stirrers and continuously rotated at about 7 rev./min. A rubber cap, acting as a valve, allowed gas exchanges, pressure measurements and the withdrawal of gas samples using hypodermic needles. The reactors were installed in a room in which the temperature was maintained at 32–33° C. with the aid of a thermostatically controlled heater and fan. Digested sludge was gassed by a mixture containing approximately 50 per cent carbon dioxide (by volume) and about 35 per cent hydrogen. A 15 per cent concentration of nitrogen was also present as an indicator since it took no part in the reaction. At the start the total gas pressure was about 30 mm. mercury above atmospheric. Biochemical hydrogen uptake diminished this pressure at the rate of 50–70 mm. mercury per day, which was dependent on the stage of the fermentation process. When necessary, every two or three days, the pressure in the reactor was restored by introduction of a further volume of hydrogen to give an approximately constant concentration of this gas in the digester. At this stage a sample of the gas was taken for gas-chromatographic investigation.

Fig. 1, which represents a series of such observations, shows that during 30 days of operation carbon dioxide concentration in the gas mixture fell from 50 per cent to about 0·5 per cent. It will be noticed that at about the tenth day methane was present in the reacting gas and that the methane steadily replaced carbon dioxide, increasing to about 50 per cent in the gas mixture.

This dynamic observation suggested the desirability of carrying out gas-chromatographic trials on the kinetics of hydrogen uptake by methane bacteria. At the conclusion of the normal methane fermentation, digested sludge was in contact with fermentation gas composed of approximately 65 per cent methane, 35 per cent carbon dioxide and traces of nitrogen. The addition of about 15 per cent of hydrogen enabled the uptake of hydrogen from this change to be observed by gas chromatography for 90 hr., after which there were no further traces of this gas.

These preliminary observations demonstrate the usefulness of the gas-chromatographic technique for such investigations. It is clear that more detailed studies, including a materials balance, are required for a full elucidation of the kinetics of these reactions.

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'Vapour Toxicity' of Solid Insecticides

When considering the performance of solid insecticides of the chlorinated hydrocarbon type, such as DDT, γ-BHC and dieldrin, a factor frequently considered is the toxic properties of the vapours from crystalline deposits. To assess this factor biologically, both in the laboratory and in the field, the commonest practice is to keep cages holding test insects a short distance from the treated surface. The toxic effect found after such an exposure is generally referred to as the 'vapour toxicity'.

However, calculation of the concentration of the saturated vapours of the insecticides mentioned above made it seem very unlikely, particularly in the cases of dieldrin and DDT, that such concentrations are high enough to cause a noticeable mortality, even of susceptible insects exposed for 24 hr. Using the equation:

$$C = (p/PV_0)M$$

in which p is the vapour pressure of the insecticide in mm. mercury, P is atmospheric pressure in mm. mercury, V_0 (the volume of ideal gas) = 22·4 l. atm. mole^{-1}, M is the molecular weight and C the concentration of the saturated vapour in grams per litre, one obtains concentration figures of 0·004, 0·53 and 0·004 μgm./l. for dieldrin, γ-BHC and *pp*-DDT respectively, the calculations being based on the results collected in Table 1. As the *LD*95 for *Drosophila melanogaster* Meig. and *Aedes aegypti* L. is of the order of 0·005 μgm./insect with dieldrin and γ-BHC,

Table 1. Vapour Pressures in mm. of Mercury

Insecticide	Vapour pressure	Temperature	Reference
Dieldrin	$1{\cdot}8 \times 10^{-7}$	25° C.	1
pp-DDT	$1{\cdot}5 \times 10^{-6}$	20° C.	2
γ-BHC	$3{\cdot}0 \times 10^{-5}$	20° C.	3

and 0·05 μgm./insect with DDT, it is not surprising that air virtually saturated with vapours of any of these three insecticides proved to be non-toxic to those insects.

The experiment was arranged as follows: Air was passed through two U-tubes filled with powdered insecticide at a rate of approximately 20 l. in 24 hr. On leaving the first tube, which was kept at a temperature of approximately 80° C., the air would be nearly saturated with insecticide at that temperature; in the second, held at about 18–20° C., the excess insecticide would recondense, leaving the air just saturated at that lower temperature. The vapour was then led through a container held at a temperature of 23–24° C., holding *Drosophila melanogaster* and *Aedes aegypti*. At this temperature the vapour is thus just not saturated. No deaths were observed among insects exposed in this way for 24 hr.

Further investigations have shown that the toxic effect often observed in experiments estimating vapour toxicity is mainly caused by insecticide acquired by the insects in an indirect way, namely, via a condensed film formed on the body of the holding cage. It is thought that appreciable condensation will take place only in a system containing saturated vapour and not in the system described above. The following experiments demonstrate the condensation phenomenon in systems with saturated vapours.

Some 10 mgm. of crystalline insecticide was evenly distributed over the bottom of a Petri dish from a solution in hexane. After evaporation of the solvent, this dish was covered by a sheet of filter paper which was larger than the rim of the dish, and covered by a second, untreated dish placed upside down on the filter paper. Care was taken that neither the filter paper nor the top dish was contaminated during this procedure. Remaining in this position overnight, the filter paper and the top dish were then separated from the dish holding the insecticide. *Drosophila melanogaster* were then exposed to the filter paper (both sides) and the top dish, the result being complete kills in all cases. Exposing metal, plastic and muslin fabric in a similar way also gave high kills of *Drosophila melanogaster* exposed to the condensed films.

The actual amounts condensed on the glass were estimated as follows: the top dishes of the combinations just mentioned (without filter paper this time) were exposed over-night to vapours from the insecticide in the bottom dish. The top dish was then removed and the condensed insecticide dissolved in hexane and dilutions of it applied on to the bottom of clean Petri dishes. Houseflies (*Musca domestica* L.) were exposed to the dry residue and the results compared with those obtained simultaneously with known amounts of insecticide. In this way the condensates of dieldrin were found to amount to a little more than 1 μgm./dm.^{2}; the condensates of DDT and γ-BHC were of the order of a few μgm./dm.^{2}. The condensates actually found on an area of 1 dm.^{2} contained, except in the case of DDT, sufficient insecticide to give a complete kill of 20 female houseflies exposed for 24 hr. With more susceptible insects such as *Drosophila melanogaster* and *Aedes aegypti*, complete mortality was also obtained with DDT.

It can be concluded from this that, in closed systems, the vapours of DDT, γ-BHC and dieldrin may condense on various materials in concentrations of a few μgm./dm.^{2}; this is sufficient to kill susceptible insects. The consequence is that where cases in the literature in general do refer to the 'vapour effect', in fact the effect is of such surface deposits of condensed vapour plus the effect of an eventual condensate directly on the insect.

It need not be stressed that this condensation can be influenced by a great number of variables, and thus that the results provided are of highly questionable value.

Thanks are due to the management of 'Shell' Research, Ltd., for permission to publish this work.

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Moisture Content of Whole Bread and Bread Crumb

In order to secure that bread is properly baked, the statutory regulations and laws prescribe maximum permissible moisture content of the baked product. In some countries the law is based on the water content of the whole loaf; in others the maximum permissible moisture content of the crumb only is laid down.

In order to compare the value of these methods in judging proper bread baking, the following sets of experiments were made (in each case with both white and high-extraction flour).

(*A*) Three pieces from one dough were scaled at 580 gm. each, fermented, panned and baked to variable final weight; (*B*) three doughs of various consistencies, and water contents, were scaled at 580 gm. and baked to a weight of 500 gm. in each case.

In all loaves the moisture content of the whole loaf and of the crumb only was determined.

Table 1. Moisture Content of Bread and Bread Crumb

No.*		Weight of baked bread (gm.)	Moisture of crumb (per cent)	Moisture of whole bread (per cent)
A	1	520	45·6	40·8
	2	500	45·4	38·4
	3	481	44·8	36·2
	4	520	45·8	41·0
	5	500	45·8	39·1
	6	480	45·9	36·0
B	7	500	46·1	39·5
	8	500	45·1	37·9
	9	500	44·6	37·6
	10	500	46·2	39·8
	11	500	45·9	37·8
	12	500	44·8	37·3

* 1–3, 7–9, dark wheat bread; 4–6, 10–12, white bread.

The results (Table 1) seem to show that prolonged baking has little, if any, influence on moisture content of the crumb, and that the latter is rather a measure of water content of dough from which the bread was baked than a criterion of adequate baking and proper crust formation.

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PHYSIOLOGY

Excretion of Catechol in Human Urine

During a study of the catechol compounds in human urine it was observed that acid hydrolysis (20 min., 1 *N* sulphuric acid, 100° C.) caused a large increase in the content of some catechol compounds, presumably by splitting of a conjugate[1]. Chromatographic separation of the different catechols obtained by adsorption on alumina of hydrolysed urine indicated that the large increase was connected with a catechol compound having a rate of flow similar to that of 3,4-dihydroxyphenyl acetic acid in a solvent system of *n*-butanol–hydrochloric acid–acetic acid[2].

Further analysis of the chromatographically separated fractions revealed that the catechol compound differed from 3,4-dihydroxyphenyl acetic acid in its migration pattern in different systems. From its position on paper when butanol–hydrochloric acid and *m*-cresol–acetic acid–water[3] were used as solvents, and by the colour observed on spraying with ferricyanide or ferric chloride, the compound was identified as catechol itself, Fig. 1. This conclusion was further corroborated by colour reactions in solution after addition of ferric chloride, by separation with ion-exchange resins and by fluorescence curves in the spectrophotofluorimeter.

The appearance in urine of a conjugate with sulphuric acid after ingestion of catechol in dogs was shown by Baumann[4] who also claimed that human urine may contain this compound. More recently, Fiker[5] has reported that hydrolysed normal urine contained 5 mgm. catechol per litre.

The amounts of catechol found in five samples of normal human urine after acid hydrolysis varied between 46 and 108 μgm./hr., and was on an average 82 μgm./hr.

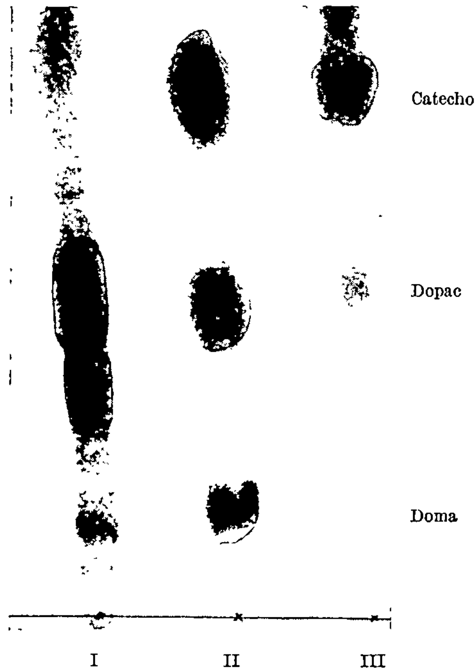

Fig. 1. Paper chromatogram, Whatman No. 1, *m*-cresol–acetic acid–water. (I) Fractions 8·8–13·2 ml. from column chromatogram of unhydrolysed normal human urine, adsorbed on alumina, solvent *n*-butanol–hydrochloric acid–acetic acid–water; (II) standards, catechol, dopac (3,4-dihydroxyphenylacetic acid); doma (3,4-dihydroxymandelic acid); (III) same as I but urine treated with 1 *N* sulphuric acid, 20 min., 100° C. before adsorption. In III about one-fifth of amount of urine in I

No evidence for the presence of catechol in unhydrolysed human urine was obtained. Catechol was also found in cow's urine after hydrolysis.

The origin and formation of the catechol are at present being studied.

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Mechanism of Action of Insulin

Experiments have been carried out to determine to what extent insulin lowers the glucose concentration in the plasma by increasing glucose utilization by the tissues and to what extent by diminishing glucose production by the liver.

Trained dogs were used in the post-absorptive state and without anæsthesia. The size of the body glucose pool and the rates of glucose production and utilization in the resting state and during periods of changing blood glucose concentrations were determined by the use of an isotope dilution technique using ^{14}C-glucose[1-3]. The body glucose pool was labelled by a priming injection of a trace amount of uniformly labelled ^{14}C-glucose. The established specific activity was maintained for several hours by a constant infusion of a trace amount of glucose labelled with carbon-14 which balanced the endogenous ^{12}C-glucose output by the liver, provided this output remained constant[1]. After the radioactive glucose had been infused for 2 hr., trypsin-treated crystalline insulin (low in glucagon content; Lilly) was administered in one of the following ways, while the labelled glucose infusion continued uninterrupted: (*a*) single intravenous injection; (*b*) continuous intravenous infusion; (*c*) subcutaneous injection. Samples of blood were collected at intervals and the plasma glucose concentration and specific activity were determined. From these results the glucose production and utilization were calculated[1,3].

It was previously shown[3] by use of this technique that when insulin is administered as a single intravenous injection the resulting hypoglycæmia is due mainly to an increased uptake of glucose by the tissues. The initial transient diminution of glucose release from the liver which was often observed was a relatively minor factor in the development of the hypoglycæmia. The return of the glucose concentration in the plasma to the control value was found to be brought about by a sudden increase in the release of glucose from the liver in response to the hypoglycæmia.

In the present studies insulin was introduced into the jugular vein through a polyethylene tube by means of a constant infusion pump. The insulin dosage varied from 0·1 to 0·25 U./kgm., infused in 90 min. In each case a hypoglycæmia developed which persisted throughout the period of insulin infusion. As shown by the relatively unchanging level of specific activity of plasma glucose the hypoglycæmia was due almost entirely to increased utilization of glucose, the glucose production remaining at about the pre-insulin level. Cessation of glucose production was never observed.

In order to determine whether physiologically secreted endogenous insulin lowers the blood sugar by the same mechanism as exogenous insulin, the secretion of insulin by islet tissue was provoked by the administration of a glucose load. The experiments were designed to provide a more adequate test than similar experiments which were reported recently[4] in which smaller glucose loads were injected in anæsthetized dogs. The body glucose pool was labelled with ^{14}C-glucose and the specific activity was maintained by a constant infusion of labelled glucose as described above. At 2 hr. a glucose load sufficient to maintain a hyperglycæmia for 45–60 min. was administered. The glucose load had the same specific activity as the glucose already circulating in the plasma. Infusion of the trace amount (less than 2 mgm./hr.) of labelled glucose was continued uninterrupted throughout the experiment. As shown by the unchanging specific activity of plasma glucose, glucose production by the liver continued during hyperglycæmia at the same rate as before the glucose load was given. The rate of glucose utilization during the hyperglycæmia was always greatly increased.

Thus it appears that physiologically secreted insulin, like administered exogenous insulin, lowers the concentration of blood sugar almost entirely by increasing utilization of glucose.

An additional finding, possibly of considerable importance, was made with regard to the restoration of the level of blood sugar after insulin-induced hypoglycæmia. The restoration of the level of blood sugar to normal, following a single intravenous injection of insulin, begins at about the lowest point of the glucose concentration curve, at which time a marked increase in glucose production occurs rather suddenly[3]. In the case of the experiments involving prolonged (90 min.) insulin infusions, this extra glucose output in response to hypoglycæmia occurred only after termination of insulin infusion, whereupon again it occurred rather suddenly and restored the blood sugar to normal.

Thus although insulin brings about hypoglycæmia primarily by increasing uptake of glucose and not by decreasing hepatic glucose output, the presence of newly injected exogenous insulin affects the animal in such a way that it fails to increase its hepatic glucose output in response to hypoglycæmia.

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Action of Pyrrolizidine Alkaloids on the Neuro-Muscular Junction

Median lethal doses of the plant pyrrolizidine alkaloids, heliotrine and lasiocarpine, have been determined by Bull *et al.*[1]. Deaths occurred from hepatotoxic effects except in some female rats given heliotrine.

The present study showed that injection of larger doses than the *LD*50 of the alkaloids, but not of their N-oxides, produced progressive muscular weakness, respiratory distress and death from respiratory failure within 30 min., suggesting the occurrence of a neuro-muscular block.

Rat phrenic nerve-diaphragm preparations were made by the method of Mogey *et al.*[2]. N-oxides of the alkaloids did not affect transmission of impulses or contraction in such preparations. However, small doses, 1–6 μM/ml., of heliotrine or of lasiocarpine first potentiated then blocked the diaphragmatic response to phrenic nerve stimulation. The lowest effective doses increased the amplitude of the contractions. With slightly higher concentrations, the initial increase in amplitude was followed by partial but progressive inhibition of contraction. Larger doses immediately inhibited contraction and rapidly led to complete inhibition. Lasiocarpine was effective in lower concentrations than heliotrine.

During complete block, the muscle responded normally to direct stimulation. Also the addition of these alkaloids to the nerve bath only, did not affect impulse transmission. The effect of the alkaloids is thus localized at the neuro-muscular junction. The block was reversed by washing the preparation free of alkaloid. However, despite the apparent complete reversal, subsequent doses of either alkaloid were potentiated. Neither prostigmin nor pentamethonium influenced inhibition due to the alkaloid or the rate of recovery from it.

The procedure outlined by Paton and Zaimis[3] was used for recording contractions of the anterior tibial muscle of cats upon stimulation of the sciatic nerve. Lasiocarpine (5–250 μM), injected into the femoral vein had no obvious immediate effect on contraction but the twitch amplitude slowly decreased. Injection of 5 and 10 μM into the isolateral anterior tibial artery increased at once the amplitude of contraction which then slowly decreased. Immediate and progressive inhibition resulted from 20 μM lasiocarpine injected intra-arterially.

The development of inhibition was not influenced by 3 mgm. potassium chloride or 0·5 mgm. pentamethonium. However, 0·25 mgm. prostigmin increased the degree of inhibition immediately. Intra-arterial injection of 25 μgm. *d*-tubocurarine produced an almost complete block of contraction which was promptly reversed by 1 mgm. prostigmin. However, the partial block produced by 15 μgm. curare did not prevent the inhibitory effect of 20 μM lasiocarpine nor was the resultant complete inhibition antagonized at all by 1 mgm. prostigmin. Tetany did not remove lasiocarpine inhibition, and contraction during tetany seemed well sustained compared with curarized muscle.

The alkaloids did not inhibit cholinesterase or the activation of acetate. The possibility of an effect on the succeeding step of acetylcholine synthesis will be investigated.

Present knowledge seems inadequate to separate agents which block impulse transmission at neuro-muscular junctions into discrete groups. With reference to the differences drawn between decamethonium-like (C_{10}-like) and *d*-tubocurarine-like compounds by Paton and Zaimis[3], the pyrrolizidine alkaloids have resemblances to, and differences from, both groups. They resemble C_{10} in the enhancement of muscle contraction in low concentrations, the failure of inhibited preparations to respond to potassium chloride, the increased inhibition resulting from prostigmin administration, the relatively well sustained contraction during tetany and failure to recover from inhibition after tetany; but they differ in the inability of the prior injection of curare to antagonize alkaloid inhibition and the failure of pentamethonium to reverse the inhibition.

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Hæmoglobin of New-born Infants in Indonesia

Studies on the hæmoglobin of new-born infants, including electrophoretic examinations, have been carried out by several workers. Normally, the red blood cells of new-born infants contain two types of hæmoglobin, fœtal hæmoglobin (Hb *F*) and normal hæmoglobin (Hb *A*). The fœtal hæmoglobin, which is resistant to alkali and has a different electrophoretic behaviour from that of normal adults, is the major component. The amount of hæmoglobin *F* in cord blood ranges from 50 to 90 per cent of the total.

In 1957, Fessas and Papaspyrou in Greece found an unusually fast-moving hæmoglobin component in a new-born infant who had symptoms of thalassæmia and whose parents were thalassæmics[1]. Nanakorn, in Thailand, reported a fast-moving hæmoglobin component in the blood of a new-born baby which she thought was hæmoglobin *H*[2]. However, this component has never been compared with the fast-moving hæmoglobin of Fessas and Papaspyrou. Agar and Lehmann reported the finding of a fast-moving hæmoglobin in a new-born baby of Chinese–Negro–Spanish–English origin, which the authors called the 'Bart's' hæmoglobin and which at *p*H 8·6 was slightly faster than that of Fessas and Papaspyrou[3].

I have continued my previous studies on the hæmoglobin of new-born infants[4,5] by making a survey of the hæmoglobin of cord blood of new-born infants in three hospitals in Djakarta. The hæmoglobins prepared from the blood samples were all examined electrophoretically by the paper electrophoretic method of Smith and Conley[6]. In many the amount of hæmoglobin resistant to alkali was estimated by the method of Singer *et al.*[7].

A total of 1,138 samples of blood was examined. 633 samples were from Chinese and Indonesian Chinese, 480 from Indonesians, 22 from Indonesian–Dutch infants, and three of other nationalities. The great majority of the samples contained normal and fœtal hæmoglobin, the alkali-resistant hæmoglobin being the major component. However, in several of the samples, a third component was present. In this material there were two kinds of an unusual third component. The first was a slow-moving hæmoglobin, while the other was a fast-moving one.

The slow-moving component at *p*H 8·6 migrated slightly faster than hæmoglobin *E* on horizontal paper electrophoresis. It was present in small quantities. Among the 633 Chinese infants (Chinese and Indonesian–Chinese), one carried this hæmoglobin in the cord blood, while the blood of 2 out of 480 Indonesian new-born babies were found to contain this component. Of the 17 Indo–European babies, one had this hæmoglobin at birth. In two of the four infants who carried a slow-moving hæmoglobin (one Indonesian and one Indo–European baby), this component was thought to be hæmoglobin *E*, because both parents could be examined and in both one of the parents had hæmoglobin *E*. The slight difference in migration-rate may be due to the relatively small amount of this hæmoglobin present. Previously[5,8] I described the postnatal formation of hæmoglobin *E* in several infants but it was not found at birth. I also noted at that time, that, when the component started to appear in the blood in a very low concentration, it migrated, at *p*H 8·6, slightly faster than hæmoglobin *E*. After some time, when the child was older, the component was present at a higher concentration. It then had exactly the same mobility as the hæmoglobin *E* in the mother. It seems from the findings in this communication that in a small proportion of hæmoglobin *E* trait carriers the hæmoglobin *E* is already detectable at birth. In the other two infants who had a slow-moving component it cannot be said that this was probably *E*, because the parents could not be examined.

The other abnormal third hæmoglobin, which was present in several of the cord-blood samples, was a fast-moving one, at *p*H 8·6 was much faster than hæmoglobin *A*, had about the same mobility as hæmoglobin *J*, but was definitely slower than *H* (Fig. 1). At *p*H 6·5 it was definitely less anodic than hæmoglobin *H*, which migrated clearly to the positive pole (Fig. 2). This hæmoglobin resembled the one

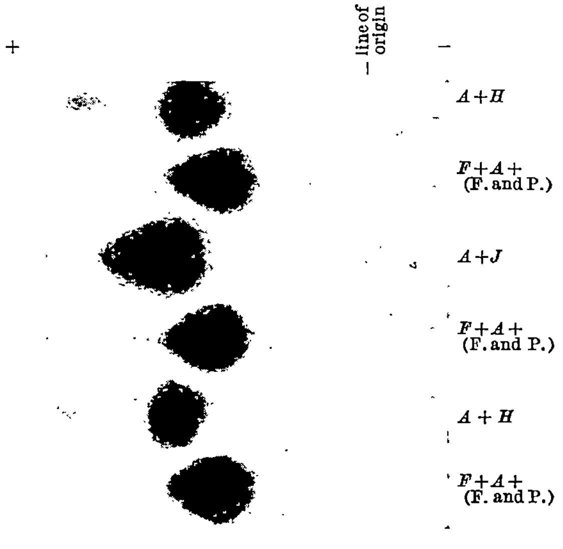

Fig. 1. Paper electrophoresis at *p*H 8·6 of the hæmoglobin of Fessas and Papaspyrou (F. and P.) in new-born babies compared with hæmoglobins *H* and *J*

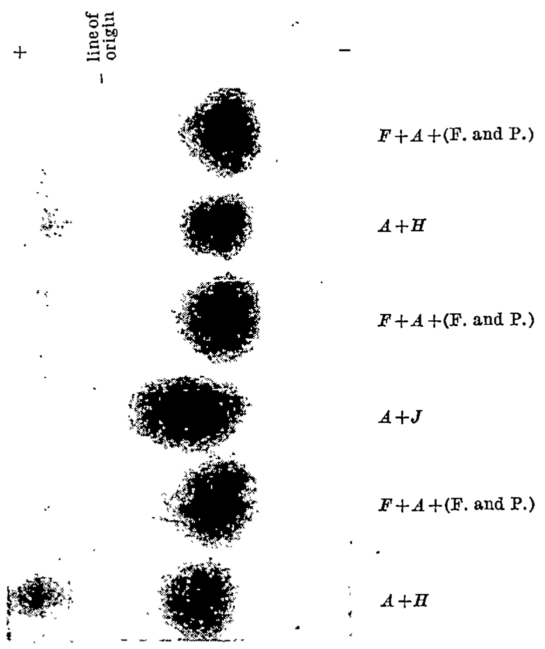

Fig. 2. Paper electrophoresis of the same hæmoglobins as in Fig. 1 at *p*H 6·5

described by Fessas and Papaspyrou in its mobility at acid as well as at alkaline *p*H. I therefore sent a sample to Dr. Fessas, who confirmed our findings and found that it was similar to that described by him and Dr. Papaspyrou. This hæmoglobin is not very stable. When kept in the refrigerator it disappeared after some time, but was more stable when frozen. It did not give rise to intracellular crystal formation in erythrocytes after several hours incubation in brilliant cresyl blue and therefore differed also in this respect from hæmoglobin *H*. A total of 23 samples was found to contain this fast-moving hæmoglobin: 21 in Chinese (among 633 samples) and 2 in Indonesian babies (among 480 samples). The parents of these babies do not have any abnormal hæmoglobin.

It seems that the hæmoglobin of Fessas and Papaspyrou is not very rare in Chinese and Indonesian new-born babies in Indonesia. Vella has found this hæmoglobin in Chinese new-born infants in Singapore[9]. It may be that this hæmoglobin is not rare in new-born infants in the whole of East Asia.

A clinical and hæmatological study was made of the babies carrying this fast-moving component and of their families. In addition, a follow-up study was made of several of the babies. The results of this study will be published separately.

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Effect of Toxopyrimidine on Glutamic-decarboxylase and Glutamic-oxalacetic Transaminase of Rat Brain

In a previous communication Rindi and Ferrari[1] reported a statistically significant decrease of γ-aminobutyric acid in the brain of rats treated with a structural pyridoxamine antagonist having an epileptogenic action, namely, 2-methyl,4-amino,5-oxymethylpyrimidine (toxopyrimidine). In this communication we wish to report results obtained in an enzymatic study of the action of toxopyrimidine. We determined the glutamic decarboxylase and glutamic-oxalacetic transaminase (both pyridoxal-phosphate linked enzymes) in the brain of rats with epileptic seizures caused by injection of toxopyrimidine, and of rats restored to normal with pyridoxamine.

The experimental conditions were as previously described[1]. Toxopyrimidine and pyridoxamine were injected intraperitoneally: at doses of 125 μgm./gm. and 62 μgm./gm. respectively.

Glutamic-decarboxylase activity was evaluated[2] by determining by paper chromatography[1] the increase in the formation of γ-aminobutyric acid in brain homogenate after the addition of glutamic acid (Table 1). Glutamic-oxalacetic transaminase was determined by the colorimetric method by Tonhazy, White and Umbreit[3] with minor modifications[4].

Table 1. Glutamic-decarboxylase and Glutamic-Oxalacetic Transaminase Activities of Brain of Rats treated with Toxopyrimidine (Mean ± Standard Error)

Glutamic-decarboxylase activity			Glutamic-oxalacetic transaminase activity		
No. of animals	Condition	Increase in γ-aminobutyric acid production (μgm.)*	No. of animals	Condition	Q_T^{10}†
10	Treated	184·7 ± 9·2	12	Treated	217 ± 4·8
8	Controls	232·2 ± 10·4	13	Controls	227 ± 8·0
11	Normals	238·5 ± 7·9	8	Normals	233 ± 13·3
6	Treated + vitamin B_6 3½ hr. after pyridoxamine	224·2 ± 9·8			
4	Treated + vitamin B_6 6 hr. after pyridoxamine	247·5 ± 7·9			

* Reaction mixture, in phosphate buffer 0·05 *M*, *p*H 6·2: (*a*) 2 ml. homogenate containing 250 mgm. of tissue + 0·5 ml. *l*-glutamic acid. 0·62 *M*, *p*H 6·2; (*b*) 2 ml. homogenate + 0·5 ml. phosphate buffer. The increment is calculated by subtracting the γ-aminobutyric acid content in (*b*) from (*a*).

† Q_T^{10}, μl.CO_2/mgm. dry tissue per hour (see ref. 3).

The results summarized in Table 1 show a statistically significant ($t = 3{\cdot}412$; $0{\cdot}01 > P > 0{\cdot}001$) inhibition of glutamic decarboxylase activity in the epileptic brain in comparison with control (and normal) animals.

3½ hr. after the injection of pyridoxamine, which quickly abolished epileptic seizures, the inhibition was completely eliminated. Since the decrease of decarboxylase activity (20·4 per cent) was of the same order[1] as the decrease in cerebral γ-aminobutyric acid (23·3 per cent) after injection of toxopyrimidine, we can assume that the two results are closely related. On the other hand, no modification in cerebral glutamic oxalacetic transaminase activity after administration of toxopyrimidine was apparent. Killam and Bain[5] reported similar results using convulsant hydrazides. They suggested that pyridoxal-phosphate is more firmly bound to the apoenzyme in the transaminase than in the decarboxylase[6,7].

Our results support the views of Tower[8], who recently emphasized the importance of the glutamic acid–γ-aminobutyric acid system in neuronal function, and the close connexion between glutamic decarboxylase inhibition and the onset of epileptic seizures in dietary or antimetabolite pyridoxine deficiency.

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Effect of Ouabain on Sodium Flux in Human Red Cells

It has been shown that the cardiac glycosides inhibit the transport of cations in human red cells[1-3], and it appears that this effect is exerted directly on the transport mechanism rather than on its energy supply[3-5]. Though some studies of the effect of these drugs on transport of sodium have been made, interest has been centred on the inhibition of transport of potassium. The present communication is concerned with the relationship between the sodium and potassium fluxes in human red cells treated with the cardiac glycoside, ouabain.

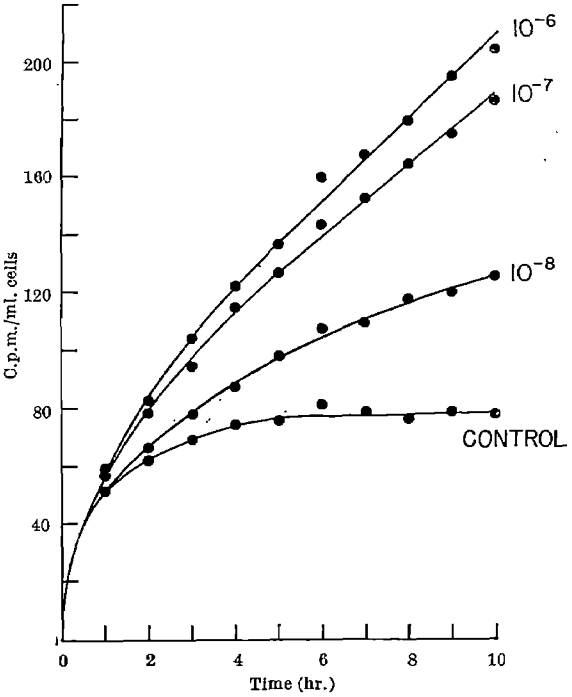

Fig. 1. Typical influx experiment showing the effect of ouabain on accumulation of sodium. Sodium chloride labelled with sodium-24 was added to fresh, heparinized human blood (relative cell volume, approximately 45 per cent)

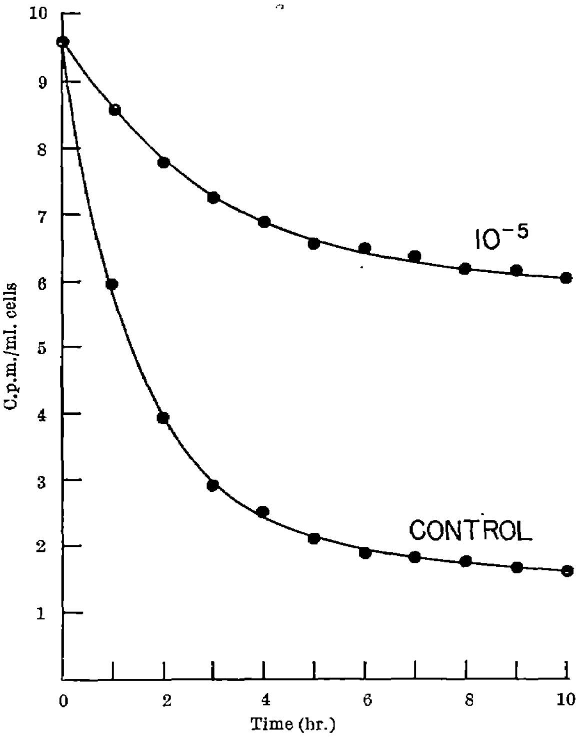

Fig. 2. Typical efflux experiment showing the effect of ouabain on sodium efflux. Fresh, heparinized human blood was incubated with labelled sodium chloride for 1 hr. The radioactive cells were separated and added to a non-radioactive, plasma-like, isosmotic medium to produce a mixture with a relative cell volume of approximately 45 per cent

Influx and efflux experiments have been carried out at 37° C. on fresh, heparinized, whole human blood using sodium chloride labelled with sodium-24 and the methods previously described[2,6]. Fig. 1 shows the results in a typical influx experiment. The concentration-range covered in eight such experiments was 10^{-4} to 10^{-11} mole ouabain/l. blood. These experiments indicate that inhibition is slight at concentrations between 10^{-11} and 10^{-9} mole/l. It increases sharply at 10^{-8} and appears to reach saturation at about 10^{-6} mole/l., though results are somewhat variable at higher concentrations.

This marked effect may represent either an increase in influx of sodium-24 or a decrease in efflux of sodium-24, since either process would result in accumulation of radioactivity in the cells. Efflux experiments (in which cells previously incubated with sodium-24 are placed in a non-radioactive medium) afford a method of discrimination between these alternatives. Four efflux experiments were carried out in the concentration-range of 10^{-5} to 10^{-7} mole ouabain/l. blood. Fig. 2, which is typical of these experiments, shows that the efflux of radioactivity does indeed decrease under the influence of the drug. From about 6 hr. onward, the efflux appears to be small and quite uniform. Thus it appears that a large portion of the gain in cell sodium-24 may be attributed to decreased efflux from the cells. A similar conclusion has been reached by Glynn[3] on the basis of a comparison of influx experiments on cold-stored human red cells with efflux experiments on normal ones.

The results for net gain of sodium may be compared with the net loss of potassium as previously measured under similar experimental conditions[2]. These

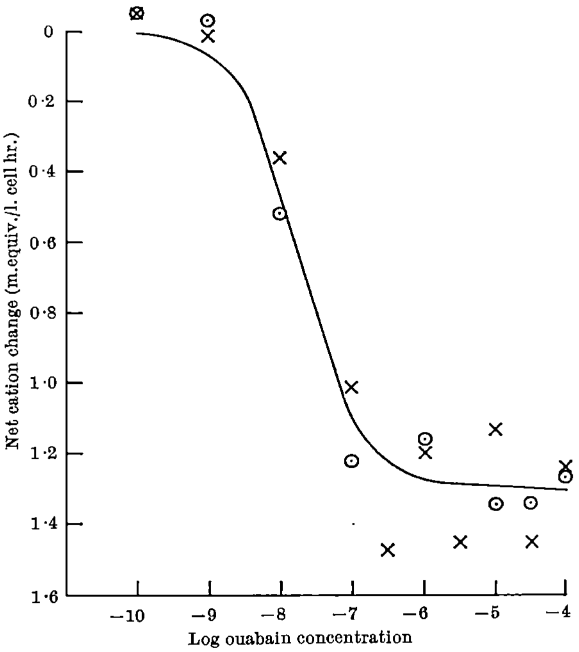

Fig. 3. Relationship between net cation shift (×, potassium loss and ⊙, sodium gain) and ouabain concentration. The results for potassium loss and the dose response curve are taken from a previous paper (ref. 2)

results are shown in Fig. 3, in which the dose response curve is that previously obtained for potassium. It can be seen that there is no demonstrable difference between gain of sodium and loss of potassium as ouabain concentration is varied over a million-fold range. 50 per cent inhibition of the affected potassium influx (which is about 80 per cent of the total potassium influx) was reached at an ouabain concentration of $3{\cdot}2 \times 10^{-8}$ mole/l. Since the curve describes the effect on sodium as well as that on potassium, the same half-inhibition value is reflected in the accumulation of sodium.

These experiments show a 1 : 1 correspondence between downhill net movements, that is, sodium influx and potassium efflux, when transport is maximally inhibited by ouabain. This makes it difficult to believe that the movement of these ions is not regulated by a common mechanism, since the electrochemical driving force is different for each cation. The correspondence is also apparent at the 50 per cent inhibition point, when processes of uphill and downhill transport both participate. Certainly, these observations could be used for supporting the proposal of Harris and Maizels[7] that red-cell sodium and potassium transport systems are linked. Glynn[8] has also reached the conclusion that there is a 1 : 1 linkage between 'active' sodium efflux and 'active' potassium influx. (Post and Jolly[9] have studied uptake of potassium by cells that have been stored at 2° C. for periods up to 25 days. They also find a linkage, 2 atoms of potassium being transported inwards for every 3 atoms of sodium transported outwards. These studies are not comparable with the present ones, since the cells had been stored for many days and their internal cation concentrations were very different from normal.) Glynn's conclusion depends upon studies of glucose-sensitive fluxes in cells suspended in a medium containing almost no potassium. These fluxes include only about half the total sodium flux; an appreciable fraction of the remainder, according to Glynn, moves by the process of exchange diffusion. The present results are compatible with those of Glynn, though ouabain may affect both Glynn's 'active' sodium efflux and the exchange diffusion process. Since ouabain apparently does not affect the supply of energy, but is presumed to act on the transport mechanism, the present results suggest that the linkage is effective at a step beyond supply of energy, probably at the cell surface, on the sites assumed important for the first step in entrance of potassium into the cell[2]. However, in both Glynn's and the present work, linkage has been demonstrated in cells that have been subject to a perturbation, such as deprivation of extracellular potassium, or the addition of ouabain. Thus, caution must be used in interpreting such observations as illustrative of the normal transport of ions across the red-cell membrane.

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Lithium Retention in Ascites Tumour Mice

Mice inoculated with an Ehrlich Lettré ascites tumour have a life-span of 2–3 weeks. In the course of ionic balance studies on such mice we noticed that these animals, after being given lithium, tended to retain more than normal controls. Daily lithium injections (1 ml. of 150 m.equiv./l. lithium chloride subcutaneously) were started on either the fifth or tenth day after inoculation, and were continued for a further four days. Food and water were given *ad libitum*. On the fifth day the mice were lightly etherized, samples of the ascitic fluid were withdrawn and blood was obtained by cardiac puncture. Plasma, red blood cells, ascites supernatant fluid and tumour cells were analysed for sodium, potassium and lithium using a Beckman flame spectrophotometer. All mice were examined for the presence of macroscopic secondary deposits.

The control mice showed a relatively constant level of red-cell and plasma lithium with this treatment. The mean plasma-level was 0·23 m.equiv./l. ± a standard error of 0·013 (15 observations). The red-cell level was 0·434 m.equiv./l. ±0·022. Thus the mean ratio of Li+(out)/Li+(in) was 0·53.

The tumour mice had consistently higher levels of plasma and red cell lithium but the results showed considerable scatter. The mean plasma lithium-level was 0·96 m.equiv./l., and the mean red-cell level was 1·15 m.equiv./l., giving a ratio of Li^+(out)/Li^+(in) of 0·83. However, the range of plasma values was from 0·27 to 2·8 m.equiv./l. The lowest plasma-level in the ascitic mice was higher than the mean control level, but we feel that the tumour mice cannot be regarded as a homogeneous population. The overall plasma to cell ratio was higher in the tumour mice than in the controls, but it was noted that where the plasma lithium-level was low the tumour mice showed a ratio similar to the controls, and as this level rose the ratio rose.

The lithium-level of the supernatant fluid obtained by centrifuging the ascites contents was very similar to that of the plasma in the same mouse. The lithium-content of the tumour cells was the same as, or slightly less than, the supernatant level. The cells appear to contain large amounts of lipid material which may complicate the estimate of ionic distribution between cells and supernatant.

The amount of trapped fluid remaining in the cell mass after 60 min. centrifugation of the ascites contents at 1,150g was estimated using radio-iodinated serum albumin, and was found to be 20–24 per cent of the total mass. This figure is somewhat greater than that found by Maizels *et al.*[1].

The mean sodium-content of the tumour cells was 75·6 ± 2·3 m.equiv./kgm. (25 observations). The mean sodium-level of the supernatant was 149 ± 2·0 m.equiv./l. and from this figure and the estimate of the trapped fluid the intracellular sodium-level was calculated to be 54 m.equiv./l. The mean potassium-level of the cells was 73·0 ± 3·1 m.equiv./l. (25), and the potassium-level of the supernatant fluid, which was very variable, gave a mean value of 18·5 m.equiv./l. Thus the intracellular potassium-level was estimated as 88·5 m.equiv./kgm. These figures are noticeably different from those found for the red-blood cell.

It will be noted that the mean supernatant fluid sodium-level is 15 m.equiv./l. lower and the mean potassium-level is 13 m.equiv./l. higher than the corresponding plasma figures. These differences may be due to ionic movements along the respective concentration gradients between the time of removal of the ascites fluid from the animal and its separation by centrifugation. This was checked in one animal by removing ascites fluid, immediately filtering some of it through a Whatman No. 42 filter paper and centrifuging the rest in the usual manner. The filtered cell-free fluid had a potassium concentration of 5·4 m.equiv./l., the same as plasma, whereas the centrifuged supernatant fluid had a potassium concentration of 7·7 m.equiv./l. This particular ascites had a cell content of 10 per cent so that the potassium leakage from the cell was of the order of 20 m.equiv./l. of the initial cell potassium. As most of the ascites in the experimental series had cell contents of 30–50 per cent the discrepancy between the supernatant fluid and plasma potassium-levels is likely to be explicable on the basis of ionic diffusion across the cell wall after removal from the animal.

The crude mean red-cell sodium was 24·4 ± 1·7 m.equiv./l., and the plasma sodium was 164 ± 2·2 m.equiv./l. (18 observations). The trapped plasma volume was 3 per cent, giving a corrected intracellular level of 21 m.equiv./l. The mean plasma potassium-level was 5·3 m.equiv./l., and the mean corrected intracellular potassium for the red cells was 123 m.equiv./l.

In general, the plasma potassium-level of the tumour mice was similar to that of the controls except in mice in the terminal stages, where levels were as high as 9·0 m.equiv./l. This was probably an agonal phenomenon.

Further experiments were carried out in which lithium was added to the drinking water at a concentration of 30 m.equiv./l. for 4 days prior to bleeding. Here again the tumour mice had higher plasma lithium-levels than the controls, and again there was more scatter in their levels than in the control animals. The control mice had mean levels of 0·77 and 0·66 m.equiv./l. lithium in the plasma and red cells respectively, compared with corresponding levels of 1·52 and 1·72 m.equiv./l. in the tumour mice. One cannot exclude the possibility of a greater lithium intake by the tumour mice in this type of experiment. It is noteworthy, however, that the ratio of plasma to red-cell lithium was higher in all drinking experiments than when the mice received lithium by injection. These mice had access to the lithium solution until immediately before bleeding, while the injected mice had their last injection some 20 hr. before bleeding. Thus the finding of a proportionately greater extracellular phase may be easily explicable.

A third type of experiment was performed to ascertain whether lithium treatment altered the ionic content of the tumour. Twelve mice were inoculated with the same sample of tumour and four days later half were given a solution of 25 m.equiv./l. lithium chloride to drink. All were killed after a further six days. We were unable to detect any significant difference in the sodium and potassium-level of the blood or the tumour between the control and treated mice. The latter had the usual lithium distribution. Under these conditions lithium does not appear to alter the ionic balance of the tumour mouse.

Given a constant intake it is clear that tumour-bearing mice retain more lithium over a period than normal controls. This must be a reflexion of decreased renal excretion in the tumour-bearing animals. It is not possible to decide from this work whether the retention of lithium is a specific renal effect, possibly hormonal, exerted by the tumour, or whether it is merely due to the mechanical effect of the accumulating ascites on the kidney. It may be that renal blood flow is greatly reduced in these animals.

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Oxidative Metabolism and Puparium Formation in the Ebony Mutant of *Drosophila melanogaster*

WE have recently reported[1] differences between the oxidative metabolism of the wild type and the ebony mutant of *Drosophila melanogaster*. (The latter has a paler and softer puparium than the wild type.) As it was found earlier[2] that dehydrogenase activity of homogenates of prepupæ at the time of pupation is 26 per cent higher in ebony than in the wild type (reciprocal values of the average decoloration time, given by homogenates of 10 prepupæ in 0·2 ml. 0·02 per cent methylene blue: 0·0469 for ebony, 0·0346 for wild), while the oxygen consumption of intact prepupæ at the same stage is only 18 per cent higher in ebony than in the wild type (average oxygen uptake per hour per 1 mgm. dry weight, 4·52 µl. for ebony, 3·71 µl. for wild type; measurements made by Miss Mary Hartman) it was inferred that during pupation the redox potential is lower in ebony than in the wild type.

As it was reported by Ohnishi[3] that tyrosinase activity at the same time is about twice as high in the wild type as it is in ebony, it was thought that these findings, taken together, support Dennell's concept[4] that tyrosinase activity is controlled by dehydrogenases, which lower the redox potential and thereby inhibit tyrosinase. Karlson and Wecker's results[5], according to which not the dehydrogenase system but rather the activity of the cytochrome system is responsible for keeping tyrosinase activity at bay, was disregarded in view of the higher percentage difference between dehydrogenase activities as compared with the difference between total oxygen consumption of the two types. This failed to take into consideration that dehydrogenase activity and total oxygen consumption are not comparable values, but the former represents only a fraction of the latter.

If we assume that total oxygen consumption is made up of dehydrogenase, cytochrome and tyrosinase activity in the same proportion in *Drosophila* as—according to Karlson and Wecker—in *Calliphora* (at puparium formation roughly half due to tyrosinase activity and a quarter each due to cytochrome and dehydrogenase activity respectively) then the 26 per cent higher dehydrogenase activity observed in ebony prepupæ would account only for a 6 per cent higher total oxygen consumption. But as this value was found to be 18 per cent higher in ebony than in the wild type at pupation, it is to be concluded that a greater part of this 18 per cent difference (roughly about two-thirds, if the ratios are the same as in *Calliphora*) must be due to a higher cytochrome activity and only a small part to a greater activity of the dehydrogenases. This indicates that the concept of Karlson and Wecker (inhibition of tyrosinase by cytochrome respiration, through competition for quinones, which are needed for the induction of tyrosinase activity), rather than the explanation of Dennell (inhibition by dehydrogenase activity and subsequent lowering of the redox potential) is the correct one.

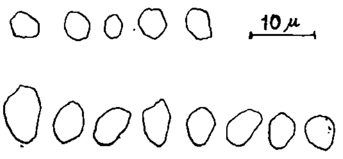

Fig. 1. Outline drawings (camera lucida) of nuclei in the corpus allatum portion of Weismann's ring. Upper row, wild type; lower row, ebony

In any event, the lower tyrosinase activity in ebony, as measured by Ohnishi and manifested in the lack of tanning of the puparium, is associated with a higher rate of respiratory metabolism. We have suggested that this increased metabolism is due to an increased activity of the juvenile hormone, produced by the corpus allatum portion of Weismann's ring, as we found the nuclei of the cells in this portion significantly larger in ebony than in the wild type (Fig. 1), and interpreted this as a sign of greater endocrine activity. The ratio of the average nuclear diameters (4·60μ for wild, 6·25μ for ebony) is almost exactly 3 : 4. Taking into consideration that somatic cells of *Drosophila*, especially those of a glandular nature (like the salivary gland cells), are known to be polytenic in various degrees[6] we venture now to suggest that the primary effect of the ebony gene is perhaps to increase the degree of polyteny in the cells of the corpus allatum portion of Weismann's ring. If this could be proved, one would have an attractive picture of the chain of physiological–biochemical processes leading from the ebony gene to the external character of the pupa, which it controls : (1) increased multiplication of chromonemata in the nuclei of the corpus allatum (either at a faster rate, or by a prolonged period) ; (2) higher degree of polyteny of these nuclei ; (3) increased synthesis of the juvenile hormone ; (4) higher rate of respiratory metabolism ; (5) greater inhibition of tyrosinase activity ; and (6) imperfect ('juvenile') tanning of the puparium.

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Inhibition of Growth and Respiration of *Ophiobolus graminis* var. *avenae* and *Aspergillus niger* by Cystine

The fungus *Ophiobolus graminis* infects the roots of wheat and barley, but does not infect oats. *O. graminis* var. *avenae*, however, infects oats as well. Both strains grow well in a simple medium containing potassium dihydrogen phosphate, sodium hydrogen phosphate, magnesium sulphate, glucose, thiamin, biotin, and a nitrogen source, usually ammonium nitrate or sulphate, or amino-acids. Most of the amino-acids give good growth when used singly as sole nitrogen source. Growth of *O. graminis* is stimulated by cysteine and cystine added to the basic medium containing ammonium nitrate up to a concentration of 0·01 *M*. Without an inorganic nitrogen salt, growth is very good with 0·04 *M* cysteine. Growth of var. *avenae* is inhibited by cystine and cysteine at concentrations as low as 10^{-6} *M* and at no concentration is growth stimulated[1]. Growth of *Aspergillus niger* is also inhibited by cystine and cysteine[2]. *Penicillium notatum* has also been described as susceptible to inhibition of respiration by cystine[3].

Some preliminary information about this inhibition in *O. graminis* var. *avenae* and *A. niger* (which both behave identically) was obtained during an attempt to correlate specificity of parasitism with metabolic differences and is reported here.

With both fungi substitution of 0·5 per cent ammonium nitrate by 0·5 per cent ammonium sulphate prevents inhibition. This protection is complete at 0·5 per cent and partial at 0·1 per cent ammonium sulphate. On adding 0·1 per cent potassium nitrate or potassium nitrite to the ammonium

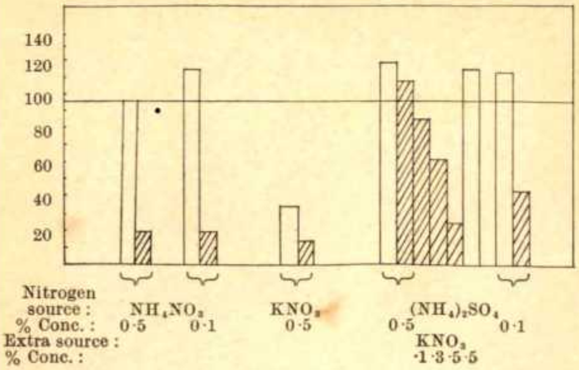

Fig. 1. Relative growth of *O. graminis* var. *avenae* showing effect on cystine inhibition of different sources of nitrogen : shaded, with 10^{-4} *M* cystine ; unshaded, without cystine

sulphate medium full inhibition again occurs (Fig. 1). The *p*H does not vary appreciably during growth in these media.

2×10^{-4} *M* aspartic acid or glycine added to the ammonium nitrate medium fully prevents inhibition by 10^{-4} *M* cystine. Serine and alanine are partially effective, other amino-acids ineffective.

Molybdenum (as sodium molybdate) added to the ammonium nitrate medium fully prevents inhibition.

Cysteine inhibits respiration of *O. graminis* var. *avenae* and *A. niger* in manometer flasks containing phosphate buffer and 2 per cent glucose only. Inhibition occurs within 30 min. of adding 2 mgm./ml. cysteine. It is equally great with no nitrogen source or with nitrate and can again be prevented by addition of ammonium sulphate (20 mgm./ml.) in absence of nitrate or nitrite ions, or of aspartate or glycine (1 mgm./ml.) or molybdenum (0·02 mgm./l.).

Table 1. CONDITIONS AFFECTING INHIBITION

Ammonium	Nitrate or nitrite	Aspartate or glycine	Molybdenum	Inhibition
		Growth experiments		
+	+			+
+	−			−
+	+	+		−
+	+		+	−
		Warburg experiments		
−	−			+
+	+			+
+	−			−
+	+	+		−
+	+		+	−

Since the inhibition by cystine is as great in the absence of NO_3^- ion as in its presence the effect of nitrate on inhibition appears to be an indirect one, in that it prevents the NH_4^+ ion exerting its usual protective effect, perhaps by interference with uptake. These observations are summarized in Table 1. The type of inhibition indicated is a metal chelation effect connected with an early stage in nitrogen metabolism. The reversal of inhibition by molybdenum suggests an effect on enzymes of the nitrate-reducing sequence[4] ; but this is difficult to reconcile with the results of the respiration experiment.

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BACTERIOLOGY

Formation of 'Protoplasts' in Mutant Strains of *Salmonella* induced by Galactose

IN 1932 Murase[1] in our laboratory isolated a peculiar mutant strain from aged broth cultures of *Escherichia coli* incubated at 37° C. This mutant had a characteristic colonial morphology on agar plates containing lactose, and because of its apparent resemblance to Massini's classical *Bacterium coli mutabile*[2] was called 'mutabile-type' by him. Since then, mutant strains having similar properties have been isolated from aged broth cultures of many strains of *E. coli*, *Shigella*, *Salmonella* and '*Paracolon*' groups, and many investigations on this particular type of mutation have been carried out in our laboratory. The results obtained may be summarized as follows[3,4].

(1) 'Mutabile-type' (*M*) mutants form convex colonies on ordinary nutrient agar plates, but when inoculated on agar plates containing galactose (or in some cases oligosaccharides containing galactose, namely, lactose or raffinose), they give rise to very flat colonies, with somewhat concave centres, and several papillæ appear on these colonies if incubation is prolonged.

(2) Wild-type strains are usually galactose-fermenting, but *M* mutants are consistently non-fermenters of galactose. (Massini's *B. coli mutabile* cannot ferment lactose, but it usually ferments galactose.)

(3) The growth of *M* mutants is strongly inhibited by the presence of even low concentrations of galactose, and this inhibition can be reversed by glucose. (Massini's *B. coli mutabile* is not inhibited by galactose.)

(4) Thus *M* mutants must be considered to be quite distinct in their nature from Massini's *B. coli mutabile*. Though *M* mutants were isolated from the aged broth cultures of many strains of the family Enterobacteriaceae, the frequency of their development varies greatly with strains used, conditions of incubation, and so on.

We have studied the mechanism of the inhibitory action of galactose on these mutants. The strain used was an *M* mutant of *Salmonella enteritidis* strain No. 11.

In the first series of the experiments, the mutant strain was grown with shaking in various liquid media—nutrient broth, salts–citrate–ammonium medium (Davis and Mingioli's minimal medium was modified by the substitution of 0·5 per cent sodium citrate for glucose), etc.—and D-galactose (Difco) was added to the final concentration of 0·1 per cent at the exponential phase of growth. Growth continued for about 30–90 min. at a slightly reduced rate, and then marked lysis was observed. But when the cells were kept in the non-growing condition, either by the addition of chloramphenicol (25 μgm./ml.) or by the removal of essential nutrients—by omitting citrate or ammonium salt from salts–citrate–ammonium medium and by omitting histidine in the case of a histidine-requiring mutant of this strain—galactose could not exert any effect on these mutant cells ; no lysis was observed and the cells remained fully viable even at high concentrations of galactose. Thus the residual growth after the addition of galactose seemed to be a prerequisite for the extensive lysis to occur. This finding, together with the facts that the M mutant cells grown in the presence of low concentrations of galactose show altered staining properties and degenerated forms[1,3,4], reminded us of some resemblance to the mode of action of penicillin on bacteria, in which case it has already been reported that: (1) penicillin induces lysis after some residual growth; (2) non-growing cells are resistant to the action of penicillin; (3) the cells grown in the presence of penicillin show various degenerate forms.

In the case of penicillin it was also reported that, when added to the suspension of *E. coli* growing in suitable hypertonic media, the bacterial cells are converted into the so-called 'protoplasts'[5,6]; spherical, osmotically fragile, yet viable (if appropriately treated) bodies. So the effect of galactose on M mutant cells was tested using a hypertonic medium. M mutant cells were grown in ordinary nutrient broth and in 'Carbowax-magnesium broth' (broth supplemented with 7·5 per cent (w/v) 'Carbowax 4,000' and 0·01 M magnesium sulphate)[7], and galactose (0·1 per cent) was added at their exponential phase of growth. As seen in Fig. 1, 'Carbowax 4,000' with magnesium ions completely prevented lysis induced by galactose. When these cells were examined under a phase-contrast microscope it was discovered that, 2–3 hr. after the addition of galactose, most of the cells in 'Carbowax'-magnesium broth were transformed into large, spherical bodies (Fig. 2), indistinguishable from the 'protoplasts' of this strain obtained by the action of penicillin in the same medium. If these 'spherical bodies' were diluted with distilled water, rapid clearing was observed, indicating their osmotic fragility. In order to confirm this finding, they were diluted serially either with distilled water or 'Carbowax'-magnesium broth, and 1 ml. aliquots of their 1 : 10^{5-7} dilutions were mixed in Petri dishes with molten 'Carbowax'-magnesium broth agar at 45° C. After overnight incubation, it was found that, when diluted with distilled water, they produced only $1 \cdot 9 \times 10^{-2}$ the number of colonies produced when they were diluted with 'Carbowax'-magnesium broth. In the control experiment with intact cells of this strain no difference in viable counts was observed between these two diluents.

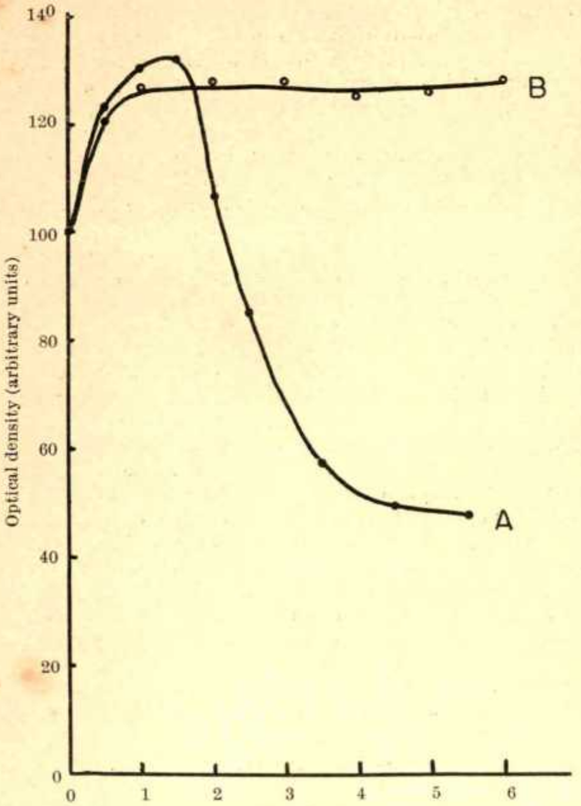

Fig. 1. Lysis of M mutant cells by galactose and its protection by 'Carbowax 4,000' and magnesium sulphate. Cells were incubated at 37° C. with gentle shaking either in nutrient broth (*A*) or in 'Carbowax'-magnesium broth (*B*). Optical density was measured at 660 mμ and expressed as relative values. The time of addition of galactose is shown as zero time

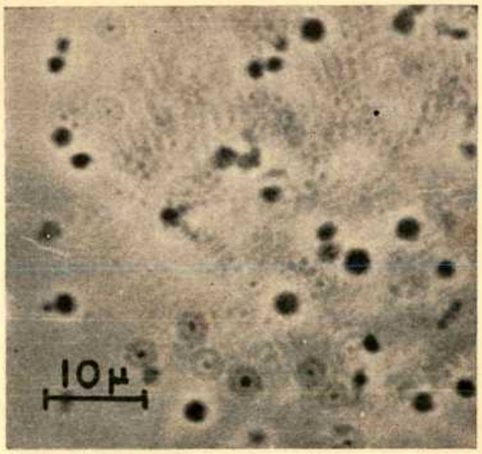

Fig. 2. 'Spherical bodies' of M mutant cells induced by galactose. M mutant cells were incubated for 2 hr. in 'Carbowax'-magnesium broth containing 0·1 per cent galactose

Results similar to those described above were also obtained with an M mutant of a strain of *Salmonella typhimurium*. As in the case with penicillin[5], the most plausible explanation of the action of galactose is the inhibition of some intermediate process of cell-wall synthesis, but other possibilities remain which cannot be excluded at present. These points are now under investigation, and will be reported later with the details of the present study.

Thanks are due to Prof. D. Ushiba and Dr. K. Kinjo for their encouragement during this work.

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Isolation of Two Types of *Pasteurella haemolytica* from Sheep

IN the course of studies on *Pasteurella haemolytica* isolated from cases of ovine pneumonia and septicæmia it has proved possible to place each strain examined so far into one of two main groups which, though closely similar, are distinguishable by certain *in vitro* characteristics. The occurrence of two types as described in this communication appears to be a different phenomenon from the colonial variation of

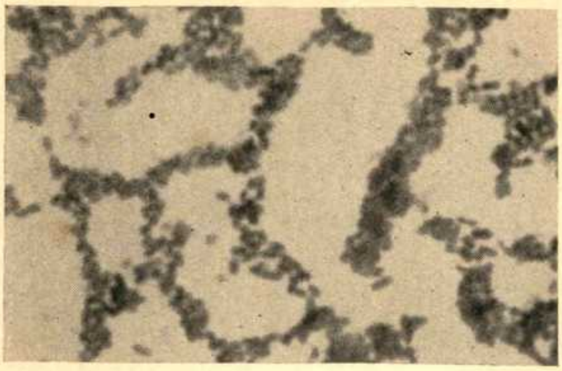

Fig. 1. Smear of T strain made in distilled water. (× 750)

Past. haemolytica recently described by Biberstein *et al.*[1]. For convenience the two forms will be referred to here as T strains and A strains, and a description of some distinguishing features is now given.

T *Strains.* 24 hr. colonies on blood agar measure up to 2 mm. in diameter. When viewed by transmitted light they are seen to possess large dark brown centres, the colour fading markedly towards the peripheries. When smears are made in distilled water from smooth colonies the bacteria generally show a strong tendency to become arranged in the lace-like pattern depicted in Fig. 1. This pattern is readily seen under the low power of the microscope. Smears made in saline show even dispersal of organisms.

Fermentation reactions are carried out in the medium recommended by Bosworth and Lovell[2]. This consists of peptone water containing 10 per cent broth with 7·5 per cent bromthymol blue and 1 per cent of the fermentable substance. The only tubes considered as positive are those which become completely yellow. All strains give a positive reaction in trehalose fermentation medium after two days incubation. The reaction in arabinose medium is negative up to the tenth day.

Growth curves in broth cultures inoculated with single colonies reach their maximum levels at about the sixth hour of incubation. The viable counts of such cultures then fall relatively slowly up to the twenty-fourth hour.

T strains are only moderately sensitive to the action of penicillin *in vitro*.

A *Strains.* Colonies growing on blood agar often tend to be rather smaller than T colonies. When viewed by transmitted light they show an even lightish-grey colour. There is sometimes a small, clearly demarcated central thickening. Smears made in distilled water usually show even dispersal of bacteria and a number of weakly staining 'ghost' forms.

All strains give a positive reaction in arabinose fermentation medium by the seventh day of incubation but remain negative in trehalose up to the tenth day.

Growth curves are different from those of T strains when broths are inoculated with comparable numbers of viable A organisms. Similar maximum viable counts are again obtained at about the sixth hour and the difference occurs afterwards as a result of the rapid and marked reduction in numbers of living A bacteria. At the twenty-fourth hour of incubation the differences in viable counts between A and T strains are only occasionally less than ten-fold and usually much greater. At this time there is no appreciable difference between turbidities of A and T broth cultures, neither is there any evidence of excessive clumping of bacteria. The pH of twenty-four hour A broth cultures is consistently slightly higher than that of T cultures.

A strains are considerably more sensitive than T strains to the action of penicillin *in vitro*.

Source of cultures. All 15 strains isolated from different outbreaks of lamb septicæmia[3] were of the T variety. No A strains have as yet been obtained from typical septicæmias. More than 20 A strains were derived in pure culture from sheep pneumonias. Four cases of pneumonia have been encountered in which mixtures of T and A strains were isolated from lung tissue, the liver, spleen and heart blood being sterile. In each of these cases A organisms predominated although the numbers of T organisms present were considerable.

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Production of 5-Keto-gluconic Acid by a Species of *Pseudomonas*

In the latest edition of "Bergey's Manual of Determinative Bacteriology"[1], several authors are cited as supporting the claim that *Pseudomonas* strains which attack glucose do so oxidatively with the production of gluconic and 2-keto-gluconic acids, whereas *Acetobacter* strains, many of which are morphologically similar to members of the *Pseudomonas*, oxidize glucose to gluconic and 5-keto-gluconic acids.

In a recent study carried out at the Torry Research Station, Aberdeen, on some fifty *Pseudomonas*-like strains of bacteria isolated by previous workers[2-4] from fish, it was found that two of these strains produced 5-keto-gluconic acid from the oxidation of glucose. In the usual peptone water plus 1 per cent glucose medium, a strong acid (but no gas) reaction was given on 3-days incubation at 30° C. These cultures reduced Benedict's reagent in a few minutes at 25° C.—a feature, according to Militzer[5], characteristic of 5-keto-gluconic acid.

The products of glucose oxidation were separated by ascending chromatography on Whatman No. 1 paper (10 in. × 10 in.), using the solvent system of McFarren *et al.*[6] (ethyl acetate/pyridine/water, 25 : 30 : 15); 5-keto-gluconic acid ran as a strongly reducing spot at R_F 0·08, easily identified with the aniline oxalate reagent of Hough *et al.*[7], with which it gives a strong yellow spot, on heating for 5 min. at 105° C. With this reagent, gluconic acid gives no reaction, and 2-keto-gluconic acid forms an intense red spot. Only the two cultures which reduced Benedict's reagent at 25° C. gave this characteristic spot.

When cultured in 0·5 per cent peptone water containing 0·5 per cent ethanol, previously sterilized by Seitz filtration, neither strain produced acid or gas, even on prolonged incubation for 3 weeks at 30° C., although growth of both was excellent after

3 days. A strain of *Acetobacter aceti* cultured in this same medium produced acid in 3 days at 30° C.

Neither strain produced pigment on any medium, but morphologically were typical *Pseudomonas* strains; they were Gram-negative, polar flagellate bacilli, attacking glucose only under aerobic conditions, using the technique developed by Hugh and Leifson[8].

Biochemically, in some fifty tests, the two strains differed from each other with respect to the following reactions: tri-butyrin hydrolysis; fucose utilization; reduction of nitrate and growth in litmus milk. In addition, one strain grew at temperatures of 0–37° C., the other 0–30° C.

It is considered that, in view of their overall similarity to each other, they should be considered strains of the same *Pseudomonas* species; and since no description of such a species appears to exist in the most recent edition of "Bergey", it may well turn out to be a new one.

A full description of the morphology and biochemistry of this species will be published at a later date.

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Synthesis of Deoxyribonucleic Acid by Phage-infected *Escherichia coli* in the Presence of Mitomycin C

IN a previous communication Shiba *et al.*[1] presented evidence that synthesis of deoxyribonucleic acid in *Escherichia coli B* was completely inhibited in the presence of mitomycin *C*, while ribonucleic acid and protein formation were unaffected as compared with that of a culture not exposed to the antibiotic. This communication shows that the impaired synthesis of deoxyribonucleic acid in cells treated with mitomycin *C* can be promptly restored by infection with bacteriophage *T2r*.

The crystalline mitomycin *C* used in these experiments was supplied by the Kyowa Fermentation Industry Co., Ltd., Tokyo, through the courtesy of Dr. S. Shiba of this University. Determinations of deoxyribonucleic acid, ribonucleic acid and protein were carried out by the diphenylamine, orcinol and Folin reactions, respectively.

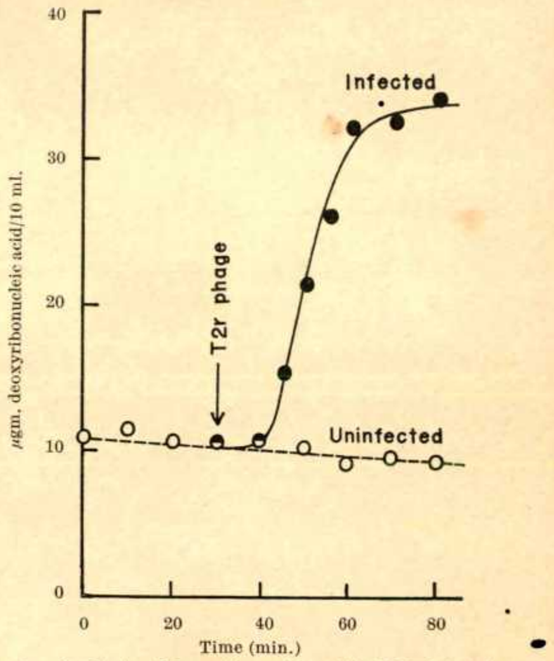

Fig. 1. Synthesis of deoxyribonucleic acid of *T2r*-infected or uninfected cells in the presence of mitomycin *C*. Cells harvested during the logarithmic phase were resuspended in fresh medium containing 10 μgm./ml. of mitomycin *C* at a concentration of 5 × 10⁸ cells/ml., and incubated at 37° C. with shaking. After 30 min., one portion of the bacterial suspension was infected with a five-fold multiplicity of *T2r* phage, and another portion was incubated without infection as control. 10 ml. aliquots of the suspension were taken at the intervals shown and analysed for deoxyribonucleic acid

Cells grown in a glucose – salts synthetic medium with aeration were harvested during the logarithmic phase, and resuspended in a similar fresh medium. Tubes containing 10 ml. of the cell suspension (series *A*, 5×10^8 cells/ml.; series *B*, 5×10^8 cells plus $2 \cdot 5 \times 10^9$ *T2r* phage per ml.; series *C*, 5×10^8 cells plus 1×10^5 *T2r* phage per ml.) with various levels of mitomycin *C* as shown in Table 1 were incubated with shaking at 37° C. for 30 min. Series *A* (uninfected cells) and series *B* (infected cells) were subjected to the assay of nucleic acids and protein. Viability of the cells and infectivity of phage were measured by plating the sample of series *C*.

As shown in Table 1, exposure of a growing culture of uninfected cells to 10 μgm./ml. of mitomycin *C* caused selectively an inhibition of the net synthesis of deoxyribonucleic acid. The level of mitomycin *C* is much higher than that proposed by Shiba *et al.*[1], indicating that the strain used in these experiments (which was kindly furnished by Dr. A. D. Hershey) was more resistant to the antibiotic. While mitomy-

Table 1. EFFECTS OF MITOMYCIN *C* ON THE SYNTHETIC ACTIVITIES, VIABILITY AND PHAGE-PRODUCING ABILITY OF *E. coli B*

Time of incubation (min.)	Concentration of mitomycin *C* (μgm./ml.)	Amount per tube						No. of viable cells (per ml.)	No. of infective phage (per ml.)
		Deoxyribonucleic acid–phosphorus (μgm.)		Ribonucleic acid–phosphorus (μgm.)		Protein (mgm.)			
		Uninfected	Infected	Uninfected	Infected	Uninfected	Infected		
0	0	12·5	13·0	62·8	62·5	0·82	0·80	$5 \cdot 1 \times 10^8$	$1 \cdot 0 \times 10^5$
30	0	18·6	37·4	93·6	66·4	1·18	1·00	$8 \cdot 5 \times 10^8$	$1 \cdot 1 \times 10^7$
30	0·1	18·7	37·2	96·5	68·9	1·20	1·01	$3 \cdot 0 \times 10^7$	$1 \cdot 2 \times 10^7$
30	1	14·2	36·9	98·7	65·0	1·20	0·95	$5 \cdot 8 \times 10^5$	$6 \cdot 9 \times 10^6$
30	10	12·3	36·2	87·7	62·8	1·18	0·98	$2 \cdot 0 \times 10^2$	$2 \cdot 4 \times 10^6$
30	100	12·1	21·4	69·2	60·2	1·07	1·00	$< 1 \cdot 0 \times 10^2$	$< 2 \cdot 0 \times 10^3$

cin C completely inhibited the formation of deoxyribonucleic acid in uninfected cells, its synthesis in cells infected by bacteriophage $T2r$ could proceed without any inhibition under the same conditions. In addition, synthesis of deoxyribonucleic acid was resumed upon infection of bacteria pretreated with mitomycin C by bacteriophage (Fig. 1). Notwithstanding the increase in deoxyribonucleic acid in cells infected by bacteriophage $T2r$, it was found that the phage titre after incubation at the same level of mitomycin C was only about 20 per cent of the control (Table 1). Although the values of phage titre given in Table 1 were for an actual multiplicity of infection of 1 (average multiplicity of 0·0002) compared with 5 for the chemical results, we have obtained similar results for phage production at the higher multiplicities.

These results are reminiscent of the facts that bacteria damaged by ultra-violet irradiation[2] or mustard treatment[3] can recover their ability to synthesize deoxyribonucleic acid when infected with phage. However, in the case of inhibition by mitomycin C, removal of the antibiotic is not required to permit the infected bacteria to synthesize deoxyribonucleic acid. Therefore, it is possible that an alternative pathway of formation of deoxyribonucleic acid, resistant to mitomycin C, may be present in the infected cells.

We wish to express our appreciation to Prof. H. Kikkawa and Dr. B. S. Strauss for their interest and encouragement in this work.

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Synthesis of Cellulose in Ethanol Extracts of *Acetobacter xylinum*

FORMATION of bacterial cellulose in cell-free fractions of homogenates of *Acetobacter xylinum*, supplemented by either adenosine triphosphate[1,2] or uridine diphosphoglucose[3], has recently been reported. Such homogenate fractions are necessarily complex, and unequivocal identification of the immediate precursor of cellulose might be easier if a cell-free extract of cultures of this bacterium, which retains the capacity to form cellulose, could be prepared. This communication describes the preparation of such an extract.

Cells free from cellulose were prepared as described by Hestrin and Schramm[4], except that they were not dried from the frozen state but stored as a suspension in phosphate citrate buffer, pH 6·0, 0·01 M in phosphate, 0·003 M in citrate. The cells from 50 ml. of suspension, containing approximately 10^9 viable cells/ml., were washed once by centrifugation with 50 ml. of 0·02 M acetate buffer, pH 5·0, and the pellet redispersed in 6 ml. of the same acetate buffer. Three 2·5-ml. aliquots of the washed cell suspension were each incubated by shaking for 5 min. at 35° C. with 2·5 ml. of 0·02 M acetate buffer, pH 5·0, plus 0·8 ml. of 2 per cent glucose in the same buffer. After incubation, each aliquot was poured into 20 ml. of rapidly stirred absolute ethanol at room temperature and the cells removed by centrifugation immediately at 15,000g. The ethanolic supernatants were recentrifuged with a small amount of incinerated 'Celite 545' (Johns-Manville Co., New York). Finally, each aliquot was passed through a glass bacterial filter, Corning 60 UF, to remove any traces of cell debris or bacterial cellulose microfibrils.

The filtered extracts were treated as follows: aliquot A was evaporated to dryness at 40° C.; aliquot B was autoclaved for 15 min. at 17 lb. and evaporated as above; aliquot C was autoclaved, mixed with 1 ml. of the ultrafiltered supernatant of a suspension of washed *A. xylinum* cells which had been incubated for 5 min. in 2 per cent glucose, and then dried at 40° C.; finally, 1 ml. of the ultrafiltered supernatant was dried at 40° (aliquot D). The four residues were digested in 4 per cent sodium hydroxide for 10 min. at the temperature of boiling water[1,3,4], to remove a fraction of the non-cellulosic substance, diluted and the insoluble material centrifuged for 15 min. at 15,000g. Pellets were resuspended in 2 ml. of water and 0·05 ml. of the suspension placed on films of 'Formvar' floating on water. After suitable dialysis to remove residual sodium hydroxide, films carrying drops were mounted on grids, dried, shadowed with palladium–gold at an angle of 15° and examined in an electron microscope. Representative electron micrographs from each aliquot are shown in Fig. 1. The remainder of the pellet from each aliquot was washed thoroughly and hydrolysed in a sealed tube at 100° in 5 per cent sulphuric acid for 16 hr. The hydrolysate was neutralized with the ion-exchange resin 'Amberlite MB 1' (Rohm and Haas) and then chromatographed in butanol/pyridine/water (10 : 3 : 3). Free sugars were detected with alkaline silver nitrate. Aliquots A and C showed only one compound, which moved at the same rate as standard glucose. Only traces of this compound were detectable in aliquot B and none from D. Autoradiographs of chromatograms from a variety of

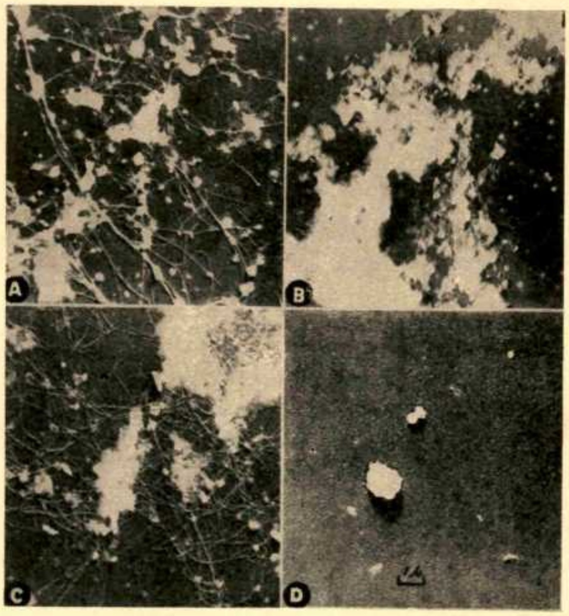

Fig. 1. Electron micrographs demonstrating formation of cellulose microfibrils from ultrafiltered ethanol extracts of active *Acetobacter xylinum* cultures: equal magnifications. Description of treatment of individual aliquots given in text

solvents, of ethanol extracts of active cultures metabolizing glucose uniformly labelled with carbon-14, so far have shown in these preparations no spots corresponding in position to those for cellobiose, cellotriose, cellotetrose, uridine diphosphoglucose or uridine diphosphate.

The fibrillar material from aliquot *A* (Fig. 1) is resistant to sodium hydroxide, yields only glucose as a component neutral sugar and has the typical morphology of bacterial cellulose microfibrils. It is formed from a precursor soluble in 80 per cent ethanol, during the evaporation of the extract, when the solution becomes predominantly aqueous. This formation of fibrillar material is almost prevented by prior autoclaving of the extract, but may be restored by addition of a portion of the extracellular medium of active cells. The precursor of cellulose microfibrils in the ethanol solution is therefore not destroyed by autoclaving for 15 min., but some accelerator of the process of microfibril formation must be. Presumably this accelerator is an enzyme. The presence of a few microfibrils in aliquot *B* indicates that the inactivation of the enzyme is not quite complete during this time. That the microfibrils do not come from the ultrafiltered supernatant of active cells is shown by the photograph of the grid from aliquot *D*. The presence of a substantial fraction of sodium hydroxide-resistant, non-dialysable, non-fibrillar material in each of the aliquots from ultrafiltered solutions should be noted because of its implications for interpretation of tracer experiments.

These results show: (*a*) 80 per cent ethanol extracts of active *Acetobacter xylinum* cells contain a compound which is converted rapidly to cellulose microfibrils when placed in water; (*b*) formation of cellulose microfibrils from this compound occurs in the complete absence of bacterial cell walls, as previously suggested[5]; (*c*) formation of microfibrils is accelerated by a heat-labile, extracellular substance in the medium of an active culture, presumably an enzyme. The results indicate also that neither uridine diphosphoglucose nor short β-glucosan chains are the immediate precursors of bacterial cellulose.

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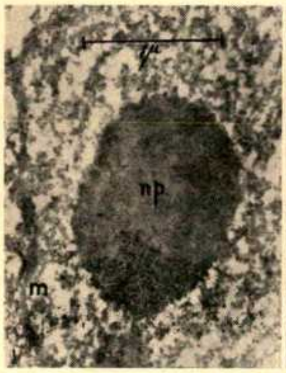
BIOLOGY

Ultrastructure of Nucleoli in Oocytes of *Patella coerulea*

A SPECIAL nucleolus, called 'Primärnucleolus' by Jörgensen[1], is always present during the growth of oocytes of *Patella coerulea*, while other nucleoli, called 'Amphinucleoli' by the same author gradually make their appearance. The 'Primärnucleolus' stains[2] red with Mallory's method and does not show the nucleolonema of Estable and Sotelo[3], while the 'Amphinucleoli' stain red at first, become blue later, show nucleolonemal elements and finally adhere to the nuclear membrane, where they gradually disappear. Previous research[4] suggested that this transition from red to blue might be due to a passage from a dense to a fluid state, which allows nucleolar substances to pass the nuclear membrane. No explanation was given of the presence of the nucleolonema in amphinucleoli and of its absence from the primary nucleolus. Electron microscope observations have been undertaken in order to check these results.

Fragments of the female gonad of *Patella coerulea* were fixed in a 1 per cent solution of osmic acid (buffered by Palade's method) and were embedded in a mixture of *n*-butyl and *n*-methyl methacrylate and sectioned with a Sjöstrand microtome. Preparations and observations were made at the Centre for Electron Microscopy at the University of Padua with a Siemens 'Elmiskop' I*a* apparatus. Throughout oocyte growth the primary nucleolus remains comparatively compact (Fig. 1) and does not present any particular structure which can be identified with the nucleolonema. It is composed of dark granules with a medium diameter of about 150 A., surrounded by granules of a lighter colour of approximately the same medium diameter (Fig. 1). These granules are more dense at the periphery. The outer surface of the primary nucleolus is not uniform, but shows strands extending into the nucleoplasm. These strands are composed of the above granules, which are also found in more or less conspicuous groups at a certain distance from the nucleolus. The same ultrastructure is shown by smaller nucleoli that are scattered inside the nucleus: they are amphinucleoli at the beginning of their formation[2].



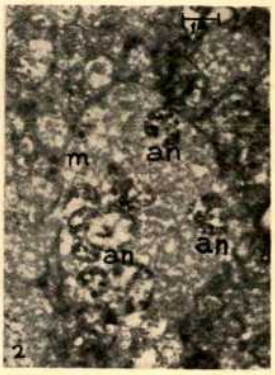


Fig. 1. Electron micrograph of the primary nucleolus (*np*) of oocytes of *Patella coerulea*; the nuclear membrane (*m*) is seen at the left. (× 9,000)

Fig. 2. Electron micrograph of the amphinucleoli (*an*) of oocyte of *Patella coerulea*; *m*, nuclear membrane. (× 2,250)

At later stages of their development the amphinucleoli have a quite different ultrastructure: they are then composed of rather thick and dark granules surrounding cavities of varying size (Fig. 2). The cavities correspond to intranucleolar vacuoles (these are also evident in later cytological preparations); the granules seem to be due to the aggregation of very small granular elements, the presence of which can also be observed in other regions of the same nucleoli. The outer surface of the amphinucleoli is more regular than the surface of the primary nucleolus.

Previous results obtained by platinum impregnation[2] are thus confirmed: during the growth of the oocyte of *Patella coerulea*, nucleoli of two types are present; one type shows evident nucleoolnemal elements, but the other type shows none.

Wischnitzer[5] observed with an electron microscope that the nucleolus of oocytes of *Triturus viridescens* "appears to maintain a compact consistency, but along the periphery strands project in all directions". He observed also that the nucleolus is formed by granules with an average diameter of about 150 A., surrounded by a matrix of lighter colour. André[6] also found that nucleoli of *Tegenaria parietina* oocytes are formed of numerous granules (100 A.) which are crowded together and form masses 0·1–0·2μ thick at the periphery. These masses are also found at a distance from the nucleolus. No mention is made of any threadlike structure resembling a nucleolonema. Finally, Serra[7], after an extensive comparative examination of nucleolar inclusions of plant meristem, oocytes of *Helix aspersa* and *Cepaea nemoralis*, and *Chironomus* salivary glands, reached the conclusion that "the nucleolonema is of the same rank as the vacuoles or other nucleolar differentiations : it is not a permanent structure in the nucleus nor does it necessarily exist in every nucleolus at all times".

However, according to Estable and Sotelo[3], the nucleolonema ought to be considered as a constant element of cellular structure. The above-mentioned results, as well as my own observations, lead to the conclusion that this is not so.

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Lens Cells of the Calf in Continuous Culture

HUMAN and animal cells of various types in continuous culture are useful for studies of cellular biology and virus-cell interactions[1]. The need for strains of primary epithelial cells suggested the calf lens as a suitable tissue for investigating the possibility of establishing such cells in continuous culture. On December 28, 1956, both eyes were removed from a 3-months-old, male calf immediately after the death of the animal. Within 5 min. after enucleation, the lenses were removed from the eyes and were washed repeatedly with Hanks's balanced salt solution. The anterior capsule was dissected by circular incision posterior to the equator and the stroma was removed from the capsule ; the epithelium remained attached to the capsule. The capsule was supplied with 2 ml. of growth medium. The latter consisted of Hanks's solution, 30 per cent calf serum inactivated at 56° C. for 30 min., 0·5 per cent lactalbumin hydrolysate and 5,000 units of penicillin and 5 mgm. of dihydrostreptomycin/100 ml. The lens capsule was gently pipetted up and down in a coarse pipette so that small fragments, about 1 mm. in diameter, were obtained. The fragments of both lens capsules were planted without plasma in two screw-cap bottles of 200-ml. size. They were allowed to be attached to the glass for 3 min. Afterwards, the flasks were provided with 4 ml. of growth medium and they were incubated stationary at 36° C. After 7 days, 4 ml. of fresh growth medium was added per flask without removal of the old medium. Thereafter, 75 per cent of the culture fluid was renewed every seventh day for two weeks and then every third or fourth day.

Four weeks after primary explantation, initial outgrowth from some explants became visible. One month later, occasional islands of transparent, scarcely visible cells were noted. Growth progressed at a very slow rate. Eleven weeks after the initial planting, cells of one flask were detached from the glass and transferred to a new flask. After this transfer the growth-rate increased and three subcultures were made by use of mechanical detachment at intervals of 2 weeks. Later, cells were detached with 0·02 per cent versene to start one sub-line and with 0·5 per cent trypsin to start another. Proliferation continued for 8 months, then began to decrease. For some months both sub-lines were maintained with difficulty and were finally reduced to one culture. The culture flask was then provided with medium containing pooled fresh calf serum inactivated at 56° C. for 30 min. Thereafter, a marked growth response was noted, and the cells have continued to proliferate at a constant rate. At the present time, cultures are divided into 2–4 subcultures after 10–14 days of incubation. The calf lens cells (strain *T–5a*) have been maintained through 44 passages for two years.

No alterations in the appearance of the cells have been observed throughout the period of cultivation. Microscopic observation of the cells shows that they are 8 to 12 times larger than other cells in continuous culture maintained in our laboratory : HeLa, human kidney and reticulosarcoma[2], mouse and rabbit kidney. Morphologically, the size and the shape of *T–5a* cells are similar to those of surviving epithelium of bovine lenses described by van den Heuvel[3]. No characteristic type of cell has been observed ; some cells are polygonal, others are pyramidal, and a number are irregular in shape. The nuclei are oval and contain several nucleoli. Long mitochondria are conspicuous throughout the cytoplasm. Intercellular bridges between cells are regularly observed (Fig. 1). In contrast to other stable cell strains, division of calf lens cells is rarely seen. Possibly these cells require a relatively short period to complete mitosis. The *T–5a* cells are remarkably resistant to the action of trypsin. After incubation for 5 hr. at 37° C. in 0·5 per cent trypsin solution, no injurious effect was noted. Attempts to cultivate the cells in a growth-medium containing less than 20 per cent calf serum and to adapt the cells to a medium of which the serum component is of heterologous origin (human and horse serum) have failed consistently. Likewise, negative results were obtained when an attempt was made to store the cells by freezing by the methods described by Scherer and Hoogasian[4].

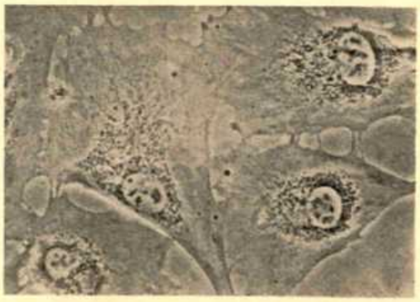

Fig. 1. Culture of lens cells of the calf (strain *T–5a*) from the twenty-fifth sub-culture ; phase-contrast. (× 560)

Poliovirus types 1, 2 and 3 did not produce degeneration of the *T–5a* cells and did not multiply in these cells either in primary culture or after passages. Adenovirus types 1–5, *7a* and 8 have been propagated serially in the cells through 5 passages with at least a 10^8-fold increase in infectivity and with reproduction of cytopathic changes similar to those in HeLa cells. The viruses caused a widespread cytopathic effect at the third to fifth day after primary inoculation. On subsequent passages, the changes were observed in a limited number of cells from the seventh to tenth day of incubation and they did not progress to complete destruction of the cultures. It is possible that the early cytopathic effect after primary inoculation is of a toxic nature, not necessarily associated with virus multiplication[5].

With the method described, we have succeeded in subcultivating cells from the lenses of two other calves (*T–5b* and *T–5c* cells). Three attempts to grow lens cells of the calf in continuous culture were unsuccessful. The *T–5b* and *T–5c* cells have been maintained through 18 subcultures for one year. No differences in morphology, growth, resistance to polioviruses and susceptibility to adenoviruses between *T–5a*, *T–5b* and *T–5c* cells were observed.

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Effect of Controlled Lighting on Production Characters in the Fowl

King[1] recently reported that a combination of restricted lighting during rearing and increasing lighting during the laying season results in increased egg production in laying pullets. Morris and Fox[2] have suggested that sexual maturity is influenced by change of length of day rather than by the absolute amount of light the birds receive during rearing. They have already published interim results[3] of an experiment which supports this contention. Their experiment also shows that decreasing lighting during the rearing of pullets hatched in December delays maturity, increases weight of eggs, but does not lower total egg production during the first sixteen weeks of lay.

Similar work, to test experimental lighting techniques, was started last year on three farms; at Glinton, Northants, at Lucan, Eire, and at Stewarton, Scotland. At all locations there are two deep-litter cabins, one with windows and one without, which can be controlled for ventilation and temperature. Each cabin contains 120 small pens, 8 ft. × 6 ft.

To apply King's method in the field it is necessary to have windowless intensive rearing houses. At the present time few people in Britain have the required facilities and it would be useful to know if increasing lighting during laying alone would produce at least part of the increase in production reported by King. This type of treatment and King's complete treatment are being tested alongside conventional lighting treatments. The treatments applied at the three locations are summarized in Table 1. The birds were reared and housed under identical conditions at each location except for the lighting treatments. There is considerable uniformity of results from several strains within each location.

The results from Stewarton, after the birds have been in lay for five months, show that the attainment of peak production is delayed, and although percentage hen-housed egg production is now higher in treated birds there is little chance of them having a higher hen-housed egg production at the end of the laying season. They have dropped too far behind in the first three months of lay to be able to catch up on the controls. At Glinton (Table 2), where the birds were housed earlier, and have been in lay six months, the treatment delayed maturity (25 per cent production) by 36 days. This could be a combination of increased age at first egg and subsequent delay in attaining normal rate of lay. The results in other respects are similar to those from Stewarton. Apart from maturity and production there are some advantages for increasing lighting. First, there is evidence that mortality is reduced. Secondly, the coefficient of variation of egg production is reduced, which on the basis of some justifiable assumptions means that heritability estimates will be increased. This could lead to improved efficiency in selection experiments carried out under these conditions. Thirdly, during the first two or three months of lay there is evidence that egg weight is increased.

At Lucan, results (Table 3) show that restricted lighting during rearing, in combination with either increasing or constant lighting during laying, leads to all the advantages listed above. Further, though maturity (25 per cent production) is delayed about 6 days compared with birds reared on natural day-length, percentage hen-housed production rises more

Table 1. Treatments Applied

Location			0–23 weeks	Housed 23 weeks onwards		
Stewarton	Control	+	Natural day-length	14 hr. a day		
	Treated	–		6 hr. a day at housing increasing by 20 min. a week		
			0–16 weeks	Housed 16 weeks onwards		
Glinton	Control	+	natural day-length	14 hr. a day		
	Treated	–		6 hr. a day at housing increasing by 10 min. a week		
			0–4 weeks	4–12 weeks	12–20 weeks	Housed 20 weeks onward
Lucan	Control	+ +	24 hr. light a day	natural day-length	natural day-length	14 hr. a day
	Treated	– +			6 hr. light a day	
	Control	+ –	24 hr. light a day	natural day-length	natural day-length	6 hr. a day at housing increasing by 15 min. a week
	Treated	– –			6 hr. light a day	

Table 2. AVERAGE RESULTS FOR STRAIN *A* AT GLINTON

	Control +	Difference	Treated −
Date hatched	19/2/58		19/2/58
Date housed	11/6/58		11/6/58
Number housed	76		74
Age at 25% hen-housed egg production in days	159	36	195
Hen-housed egg production to 31/12/58	84·4	12·1*	72·3
Coefficient of variation of hen-housed egg production (%)	12·3	7·5	4·8
Hen-housed egg production December 1958 (%)	46·9	13·8	60·7
Mortality (%)	3·9	1·2	2·7
Egg weight, oz./doz. October	24·0	0·7*	24·7
Egg weight, oz./doz. November	24·0	1·4†	25·4
Egg weight, oz./doz. December	24·7	0·8†	25·5

* Significant, $P < 0·05$. † Significant, $P < 0·01$

Table 3. AVERAGE RESULTS FOR STRAIN *M* AT LUCAN

	Control + −	Difference	Treated − −
Date hatched	28/4/58 to 12/5/58		28/4/58 to 12/5/58
Date housed	26/9/58		26/9/58
Number housed	485		486
Age at 25% hen-housed production in days	162	6	168
Hen-housed egg production to 31/12/58	42·3	8·5†	50·8
Coefficient of variation of hen-housed egg production (%)	18·0	5·8	12·2
Hen-housed egg production for December 1958 (%)	56·8	18·0	74·8
Mortality (%)	2·9	1·5	1·4
Egg weight, oz./doz. October	19·4	0·6*	20·0
Egg weight, oz./doz. November	22·2	0·3	22·5
Egg weight, oz./doz. December	23·4	0·3	23·1

* Significant, $P < 0·05$. † Significant, $P < 0·01$.

sharply and reaches a higher peak. At the end of three months in lay, total egg production and percentage hen-housed production are higher in the birds which received restricted lighting.

If the hypothesis put forward by Morris and Fox[2] is correct, it is the change in length of day from one day old to housing, rather than restriction of light, which has brought about the consequent improved production. The pullets at Lucan, in fact, dropped from 24 hr. light a day during the first month to 6 hr. a day at housing. According to the formula given by Morris and Fox[3] this should delay maturity by 13 days compared with the control group. Their formula was calculated from data on Rhode Island Red × Light Sussex chickens and refers to age at first egg. The present observations refer to age at 25 per cent production, and, therefore, a comparison is not justifiable. However, the amount of delay may depend on whether the change in light during rearing is applied gradually, or, as in the experiment reported here, in a two-phase reduction.

Records from the birds at Glinton, Lucan and Stewarton will be collected for a ten-month laying season. The details and results of the experiments will then be published in full elsewhere, at a later date.

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Sex Incidence of Vascular Lesions in Aging Rats in Relation to Previous Pregnancies

Wexler and Miller[1], in describing the production of severe arterial sclerosis in rats treated with corticotrophin, noted the greater susceptibility of their 1-year old breeding females to these lesions. We have found that during and between pregnancies, human uterine arteries undergo profound alterations, including 'reduplication' of internal elastic laminæ and massive intimal mucopolysaccharide accumulation. That alterations occur in pregnant women, not only in uterine but also in other arteries throughout the body, is suggested by the relationship which has been shown between pregnancy and aortic aneurysms or ruptures[2]. We therefore decided to investigate the spontaneous incidence of vascular injuries in breeding and non-breeding male and female stock rats in our colony. These animals consumed our standard diet, which permits normal growth, breeding performance and life-span.

The incidence of aortic and coronary mineralization in 81 untreated stock rats over the age of 500 days is shown in Table 1. It will be seen that these lesions were absent among male rats, occurring only in females ($P < 0·01$), and that among the latter the lesions were much more common in breeders than in non-breeders ($P < 0·02$). These discarded breeding females had all had 3–7 litters each.

Table 1. INCIDENCE OF BOTH AORTIC AND CORONARY MINERALIZATION IN STOCK RATS

(No. of rats with lesions/total rats in group)

Age group (days)	Male		Female	
	Non-breeders	Breeders	Non-breeders	Breeders
501–800	0/10	0/5	0/13	6/15
801–1,240	0/18	0/5	2/7	4/8
Total	0/28	0/10	2/20	10/23

Mineralization (calcium and/or iron 'coating') of the internal elastic membranes of smaller vessels, such as the coronary, mesenteric and uterine arteries, was common in these discarded breeding females, as was the deposition of iron in the basement membranes of the proximal convoluted tubules of the kidneys, and even in the depot fat cells. The aortæ (ascending, thoracic and abdominal) were, however, most severely affected in all instances (Figs. 1 and 2), and showed rigidity and calcification, and even cartilage and bone formation, together with the intimal and medial fibrosis, ectasia and heavy mucopolysaccharide accumulations mentioned by Wexler and Miller in their animals treated with corticotrophin. Calcification, with heavy mucopolysaccharide accumulations and cartilage formation was common in the papillary muscles of both ventricles, and this was associated with moderate fibrosis of the underlying myocardium. Increases in pericoronary reticulin were notable and, although gross infarcts were not found, patchy increases in myocardial reticulin were common. However, the coronary arteries themselves were not as seriously damaged in our untreated old breeding females as was apparently the case in Wexler and Miller's animals treated with corticotrophin; coronary thromboses were not seen by us, although the coronary vessels were unduly dilated, rigid and mineralized in our breeding females.

These lesions occurring spontaneously in breeding females were indistinguishable from those described

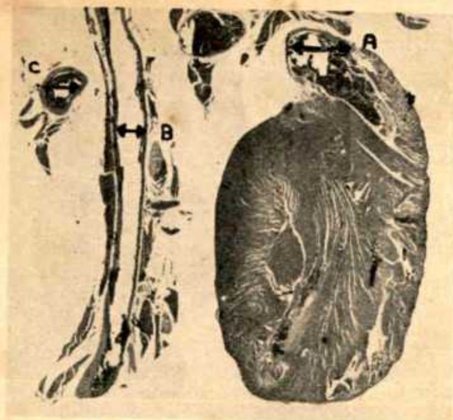

Fig. 1. Heart, ascending aorta (*A*) and thoracic aorta (longitudinal, *B*, and transverse section, *C*) to show cardiac size and aortic diameter (compare with Fig. 2). Stock non-breeding female 797 days old. Stained von Kossa. (× 3·6)

in healing arteries after short-term toxic doses of calciferol[3-5] as was the close association between mucopolysaccharide accumulations and mineral deposition and fibrosis. Selye[6] has shown that corticoids markedly increase the susceptibility of the coronary arteries in rats to similar acute traumata. The corticotrophin treatment applied by Wexler and Miller may thus have aggravated pre-existing cardiovascular lesions in their breeding females.

Closer attention to endocrine and other factors influencing the integrity of arterial walls during growth and under various physiological conditions, including pregnancy, certainly seems merited. Sex hormones have been shown to regulate circulating fibrin and fibrinolysins[7], anticoagulants, and even more powerful thrombolytic substances perhaps appearing in the circulation during pregnancy. The ovarian hormone relaxin, known to promote lysis of ligaments and even bone in œstrogen-primed animals, may affect arterial structure during pregnancy. The effects of endocrine glands, and of pregnancy in particular, in 'protecting' some arteries while promoting degeneration and subsequent intimal fibrosis, thrombosis or even rupture in others, thus merits experimental study and epidemiological surveys in man.

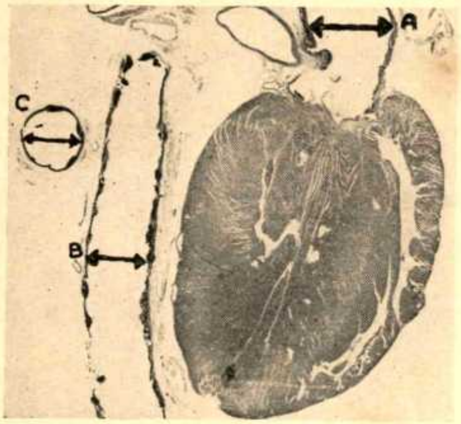

Fig. 2. Section similar to that in Fig. 1 but from 636-day-old female that had had five litters. Note enlarged heart, grossly dilated ascending aorta (*A*) and thoracic aorta (*B* and *C*). The black material in the aorta (*A*, *B* and *C*) is von Kossa-positive material (calcium); iron was also demonstrated in these areas. (× 3·6)

We wish to thank the Schlesinger Organization and the Wellcome Trust for generous financial assistance, and Mrs. P. Kruger, Miss A. Killerby and Miss M. D. Carolan for their assistance.

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Amniotic Fluid and the Fœtal Lung

OF the problems associated with development of mammalian fœtal lungs, and with the changes they undergo just before and at birth, many are controversial, but Gairdner[1], in his careful review of the subject, states that "the weight of evidence supports the view that the fœtus normally inhales and absorbs liquor amnii".

During an investigation into the microscopic appearances of rat fœtal lungs following a variety of experimental procedures, I have been able to make an observation which not only throws considerable doubt on the hypothesis of Potter *et al.*[2] and Policard *et al.*[3] that the inhalation of amniotic fluid is a normal and necessary morphogenetic factor in the expansion of the alveolar spaces, but which also provides positive evidence of actual production of fluid by the fœtal lung, such as has occasionally been postulated.

Rat fœtuses were operated on *in utero* between the seventeenth and nineteenth days of gestation (the day of finding sperm in the vaginal smear being counted as day 1). The uterus was afterwards opened under pentothal anæsthesia in a warm saline bath some hours before the time for normal parturition on the twenty-second day. With minimal handling, and provided the placental circulation remained intact, both normal and experimental fœtuses invariably lay inert in the saline; in this state they were injected with either morphine sulphate or D-tubocurarine chloride in order to prevent the subsequent occurrence of gasping movements, which are capable in themselves of altering profoundly the appearances of intra-thoracic viscera. Fixation in Helly's fluid was followed by paraffin-embedding and serial-sectioning of the neck and thorax.

The aim of the first operation was to transect the trachea through an orientated stab-incision in the uterine wall. Survival-rates of operated fœtuses were as follows:

2-day survival	10 out of 17 operated
3-day survival	9 out of 14 operated
4-day survival	11 out of 36 operated

Preparation and study of the serial sections is now in progress. Operated animals show retardation in body-growth compared with normal controls, so that a twenty-second-day experimental fœtus usually corresponds approximately to a twenty-first-day control. Most of the 16 specimens so far studied in detail show little evidence of damage at the site of

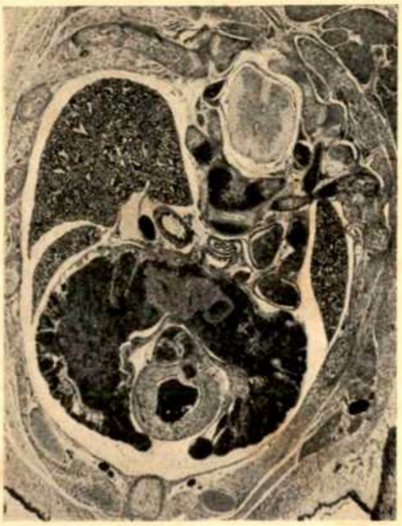

Fig. 1. (× 8)

incision. In some cases this may be because the transection was incomplete; but many of these specimens show marked accumulation of cells and cell-debris in the pharyngeal lumen: it is well known that fœtal tissues show remarkable powers of regeneration, especially when, as in these cases, the edges of the wound are left in close apposition.

Fig. 1 shows the thoracic viscera in transverse section at a standard level in such a fœtus on the twenty-second day, 4 days after the neck was incised. The microscopic appearances of the lungs are very similar to those in a normal twenty-first-day fœtus. Fig. 2 is a similar section from a litter-mate which had been operated on at the same time. In this specimen the margins of the incised trachea had failed to re-unite; in the serial sections there is a gap of 240μ between the blind ends of the proximal and distal portions of the trachea. The lungs were therefore isolated from the amniotic sac. Despite the small size of the animal and of its lungs, the latter are expanded to a degree greater than in a normal twenty-second-day fœtus. There is, in addition, a marked effusion into the pleural cavity, which is perhaps reasonably interpreted as the result of transudation from the overfilled alveolar spaces.

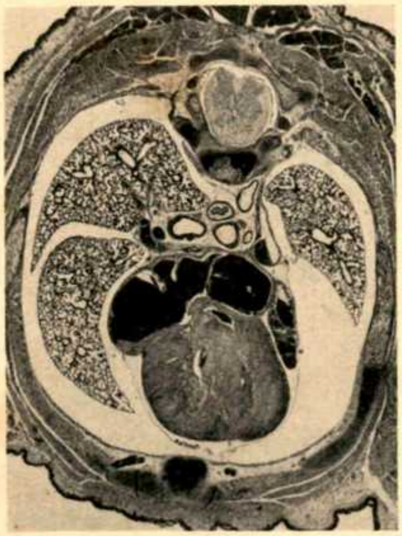

Fig. 2. (× 8)

It is concluded that the fœtal lung is capable of producing whatever fluid is necessary to fill the enlarging alveolar spaces. The fluid appears to be produced in excess, and this would favour the view of Whitehead *et al.*[4] that the lung is itself one of the sources of amniotic fluid. This conclusion is not necessarily true, however, and it is considered likely that any excess fluid would normally enter the pharynx and be swallowed by the fœtus.

This interpretation of experimental findings would appear to give a rational explanation for the similar appearances reported by Potter *et al.*[5] in a case of a human accessory lung without connexion to the trachea, and by Jost and Policard[6] in rabbit fœtuses previously subjected to decapitation. These authors were unable to account for their findings on the basis of their published views on the morphogenetic factors involved in normal fœtal lung-growth and expansion.

Work on this series, and other experiments on fœtal lungs, are still in progress.

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Testing Populations of Beet Eelworm, *Heterodera schachtii* Schmidt, for Resistance-breaking Biotypes, using the Wild Beet (Beta *patellaris* Moq.) as Indicator

SOME species of wild beet, including *Beta patellaris*, are resistant to beet eelworm. The roots of *B. patellaris* are invaded by larvæ, a small proportion of which develop into mature males, but usually no mature females are produced[1].

Dunnett[2], Jones[3], Goffart[4] and Huijsman[5] found that some populations of the potato root eelworm, *H. rostochiensis* Woll., from various parts of Britain, Germany and Peru reproduce in the wild potato, *Solanum tuberosum* sub sp. *andigena*, which had been resistant to the populations previously tested. Populations of beet eelworm from various parts of England were therefore tested on *B. patellaris* to see whether any could be found able to produce cysts on this species.

Eight populations were tested from the following districts: Iffley, Oxon.; Soham, Cambs.; Waterbeach, Cambs.; Lakenheath, West Suffolk; Chatteris, Isle of Ely; Spalding, Lincs; Oxlode, Isle of Ely; Yeovil, Somerset. Plants of *B. patellaris* were grown singly in potting compost in 6-in. pots, plunged in gravel. Replication was three-fold and 4,000 hatched larvæ were added per pot.

Ten weeks after adding the larvæ, the tops were removed and the soil and roots air dried. Cysts were recovered by elutriating the soil[6] to ensure that all cysts present were detected.

A single cyst was found from one plant in each of the Spalding and Yeovil populations and two cysts from one plant in the Oxlode population. This is the first record of the development of females on *B. patellaris*.

Thus, although there is no evidence of resistance-breaking biotypes occurring on the same scale as found with *H. rostochiensis*, individual females able to develop on *B. patellaris* exist and their potential importance should be recognized. Further investigations are needed on the extent to which these biotypes can give rise to populations containing a larger proportion of such individuals. As one of the possibilities considered in breeding sugar beet resistant to beet eelworm is to introduce genes for resistance from *B. patellaris*, a situation favouring the multiplication of these biotypes might result from growing sugar beet × *B. patellaris* crosses in the field.

This work was carried out at the School of Agriculture, Cambridge, and financed by the Sugar Beet Research and Education Committee.

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Persistence of Tomato Aucuba Mosaic Virus in Dried Leaf Tissue

IN December 1934, in order to keep in a convenient form some material of the strain of tomato aucuba mosaic virus with which I had been working at Rothamsted Experimental Station, some leaves of infected tomato plants were dried in air and put in an envelope.

After I came to this Department, some of this material was used from time to time for inoculating plants in connexion with the experiments being carried out here. The original virus has been transmitted from plant to plant by juice-inoculation for the past 24 years.

The envelope containing the original material (of December 11, 1934) was kept in a cupboard in the laboratory, and it was thought that it would be interesting to see what had happened to the infectivity of the virus after a period of desiccation of 24 years.

A small leaflet weighing 10 mgm. was crushed in a mortar and 10 ml. of water added and the whole thoroughly mixed. After 1 hr., an interval to allow of complete wetting of the dry material, about 0·1 ml. of liquid was rubbed on to each of 16 leaves of plants of *Nicotiana glutinosa*.

The control material was a fresh leaflet of tomato of approximately the same size as that selected for the first experiment. This was infected with the same strain of virus which through the years has been inoculated from tomato to tomato plant.

This material was again thoroughly macerated, mixed with 10 ml. water and left for 1 hr. at laboratory temperature. Similar amounts of liquid were inoculated by rubbing with a finger into each of 16 leaves of *N. glutinosa* plants. The results were as follows :

Material	Total number of lesions on 16 leaves
Dry material (Dec. 24, 1934)	2 + 1 (doubtful)
Control material (fresh)	652

The experiment was repeated using 200 mgm. of dried material in 10 ml. of water. Similar amounts were rubbed on to each of 14 leaves of *N. glutinosa* plants when it was found that, after an interval of 5 days, a total of 15 + 2 doubtful lesions had developed on the 14 leaves.

This same material was left for 24 hr. to allow further wetting of the dried material if this were necessary, and five lesions were found on fifteen leaves of *N. glutinosa* after inoculation and treatment similar to that noted above.

It appears, therefore, that while the activity of the tomato aucuba mosaic virus is very greatly reduced by desiccation and storage in a dry state for 24 years, there is still a little residual activity even after that period of time.

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A Third Species of 'Pepper' in West Africa

Two workers on the peppers (*Capsicum*), Smith and Heiser[1], have recently discovered that among the peppers of Central and South America a new species of pepper, *Capsicum sinense* Jacq. had been present within the species *C. frutescens* L. This new species, which could not at first be detected when *C. frutescens* was itself separated from *C. annuum* L., is now recognizable by the 3–5 flowers at each node, the declinate pedicels, and the circular constriction at the base of the calyx in fruit, quite apart from the sterility barrier between it and the four other species of pepper in Central and South America, namely, *C. pubescens* R. and P., *C. annuum* L., *C. pendulum* Willd., and *C. frutescens* L.

This discovery calls for a verification in other parts of the world where the peppers flourish to see if this new species could be found there. West Africa is certainly one of the areas that are rich in peppers which form an important item of the local dish ; but only two species *C. annuum* L. and *C. frutescens* L. have been described[2]. For well over a year now, collection of local varieties of peppers have been made in West Africa with special reference to Ghana. More than sixty varieties have so far been cultivated and described (unreported), and the results show that the new species *C. sinense* is present also in West Africa. Two distinct varieties of this species have so far been distinguished, and these will be described separately elsewhere. Nothing has been found among the collection to answer to any of the other two species in Central and South America. This third species of pepper, *C. sinense*, in West Africa will have to be included in the "Flora of West Tropical Africa" now under revision.

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FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Monday, April 20

British Society for the Philosophy of Science (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. W. C. Salmon: "The Concept of Empirical Verifiability".

Society of Chemical Industry, Pesticides Group (at 14 Belgrave Square, London, S.W.1), at 5.30 p.m.—Annual General Meeting, followed by Dr. F. Call: "The Chemical Control of Nematodes in Soil".

Royal Society of Arts (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Prof. J. B. Speakman: "Research in Wool". (First of three Cantor Lecturers. Further lectures on April 27 and May 4.)

Monday, April 20—Tuesday, April 21

Electrical Association for Women (in London)—Thirty-fourth Annual Conference. Theme: "Education in a Scientific Age". Speakers: The Rt. Hon. Reginald Maudling, M.P., The Countess Mountbatten of Burma, C.I., G.B.E., D.C.V.O., Ll.D., and Lady Bragg, M.A., J.P. Chairman: The Viscountess Kilmuir, D.B.E.

Monday, April 20 (at the Federation of British Industries. 21 Tothill Street, London, S.W.1), from 2 p.m. to 5 p.m.—Branch Officers' Session.

Tuesday, April 21 (at the Connaught Rooms, Great Queen Street, London, W.C.2), at 10.30 a.m.—Annual General Meeting.

Monday, April 20—Friday, April 24

Industrial Photographic and Television Exhibition and Conference (at the Royal Albert Hall, London).*

Tuesday, April 21

Royal Aeronautical Society (at the Institution of Mechanical Engineers, Birdcage Walk, Westminster, London, S.W.1), at 9.45 a.m.—All Day Discussion on "The Structural Effects of Kinetic Heating".

Institution of Electrical Engineers, Measurement and Control Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Discussion on "The Problem of Maintenance of Electronic Equipment in the Process Industries", opened by Dr. G. Morris and Mr. N. T. C. McAffer.

Wednesday, April 22

Institute of Fuel (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 6 p.m.—Mr. T. C. Bailey: Presidential Address.*

British Institution of Radio Engineers (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Dr. D. J. E. Ingram: "The Application of Magnetic Resonance to Solid State Electronics".

Women's Engineering Society, London Branch (at Hope House, 45 Great Peter Street, London, S.W.1), at 7 p.m.—Mr. A. B. McKenzie: "Development of the Gas Turbine Aero Engine".

Thursday, April 23

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Meeting for Election of Foreign Members, followed by Miss Elizabeth Rhodes and Prof. A. R. Ubbelohde, F.R.S.: "Melting and Crystal Structure. Effects of Thermal Transformations of Ionic Crystals on their Ultra-violet Absorption"; Mr. B. Szigeti: "Higher Order Terms in the Dielectric Constant of Ionic Crystals".

Royal Society of Arts (at John Adam Street, Adelphi, London, W.C.2), at 5.15 p.m.—Mr. S. H. U. Bowie: "The Uranium and Thorium Resources of the Commonwealth".

Institution of Electrical Engineers (at Savoy Place, London, W.C.2), at 5.30 p.m.—Sir David Brunt, F.R.S.: "The Geophysical Year 1957–58" (Fiftieth Kelvin Lecture).

British Glaciological Society (at Bedford College, Regent's Park, London, N.W.1), at 6 p.m.—Annual General Meeting. Mr. C. W. M. Swithinbank: "Sea Ice in the North West Passage over the last 58 Years".

Royal Aeronautical Society (at the Institution of Mechanical Engineers, Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Mr. W. H. Stephens: "Earth Satellites".

Friday, April 24

Linnean Society of London (in the Lecture Theatre, British Museum (Natural History), Cromwell Road, South Kensington, London, S.W.7), from 10.30 a.m. until 6 p.m.—Meeting on "Comparative Studies in Ultrastructure". Speakers include Dr. George E. Palade, Dr. Sanford L. Palay, Dr. J. Hanson, Dr. H. E. Huxley, Dr. J. Lowry and Mr. Andrew F. Huxley, F.R.S.

Institution of Electrical Engineers, Radio and Telecommunication Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. T. C. Macnamara and Mr. B. Marsden: "Engineering Aspects of Commercial Television Programme Presentation".

University of London (in the Anatomy Lecture Theatre, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. O. Heckmann (University of Hamburg): "Some Current Observing Programmes of the Hamburg Observatory". (First of three Special University Lectures in Astronomy. Further lectures on April 27 and 29.)*

Institution of Mechanical Engineers (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Annual Meeting.

Friday, April 24—Saturday, April 25

Royal Society of Medicine, Endocrinology Section and the Society for Endocrinology (with the participation of the Society for the Study of Fertility, the Medical Section of the British Diabetic Association, the London Thyroid Club, and the Endocrine Club, Glasgow, at the Royal Society of Medicine, 1 Wimpole Street, London, W.1)—Joint Endocrine Meeting.

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Assistant Lecturers (honours graduates in physics or chemistry) in Polymer Chemistry—The Registrar, Manchester College of Science and Technology, Manchester 1 (April 25).

Secretary (preferably with a professional qualification and experience in grant-aided work) of the Welsh Plant Breeding Station, to be responsible for the administration, accountancy and office organization—The Registrar, University College of Wales, Aberystwyth (April 25).

Lecturer, and a Lecturer (Grade B) in the Mathematics Department—The Secretary, Northampton College of Advanced Technology, St. John Street, London, E.C.1 (April 27).

Assistant Lecturer or Lecturer in the Department of Zoology—The Registrar, The University, Liverpool (April 28).

Senior Principal Scientific Officer (with a first- or second-class honours degree in chemistry, chemical engineering or physics, or equivalent, or high professional attainment, and practical experience in mineral dressing and/or hydrometallurgy) at Warren Spring Laboratory, D.S.I.R., Stevenage, Herts, to lead a section carrying out research on mineral processing—The Civil Service Commission, 17 North Audley Street, London, W.1, quoting Ref. S.4964/59 (April 28).

Assistant Lecturer in Physics—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (April 30).

Assistant Lecturers or Lecturers in Civil or Mechanical Engineering—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (April 30).

Geologist (with an honours degree in geology requiring a four-year course at a recognized university, and preferably with previous experience) with the Government of Southern Rhodesia—The Secretary (R), Rhodesia House, 429 Strand, London, W.C.2 (April 30).

Lecturer in Physics—The Registrar, King's College (University of Durham), Newcastle-upon-Tyne (April 30).

Lecturer (with a special knowledge or experience of physical methods, and the ability to teach to honours standard, and to initiate and supervise research) in Pharmaceutical Chemistry—The Secretary-Treasurer, Royal College of Science and Technology, Glasgow (April 30).

Plant Physiologist or Botanist (with an honours degree in botany, and preferably postgraduate experience in plant physiology, biochemistry, or with herbicides) to evaluate new herbicides in greenhouse and pot culture studies and to determine their phytotoxic properties; and an Agronomist or Horticulturist (with an honours degree in agriculture or science with postgraduate training or research experience), to take charge of part of the field evaluation programme on new herbicides—Dr. E. K. Woodford, A.R.C. Unit of Experimental Agronomy, Department of Agriculture, Oxford (April 30).

Assistant Lecturer in Physics—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 1).

Assistant Lecturer or Lecturer (well qualified in systematic geography, and preferably first-hand knowledge of a region other than Western Europe) in Geography—The Assistant Registrar, The University, Edmund Street, Birmingham 3 (May 2).

Lecturer (with special qualifications and research experience in fruit growing) in Horticulture—The Registrar, Room 22 (O.R.B.), The University, Reading (May 2).

Lecturer in Physiology—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 4).

Assistant Lecturer (with special interests in crop production and the mechanization of crop production) in Agriculture—The Registrar, Wye College (University of London), near Ashford, Kent (May 5).

Chair of Physics—The Registrar, University College of North Staffordshire, Keele, Staffs (May 9).

Lecturer in the Department of Mathematical Physics—The Secretary, The University, Edinburgh (May 9).

Senior Lecturer and a Lecturer in the Department of Biochemistry—The Secretary, The University, Edinburgh (May 9).

Assistant Lecturer or Lecturer in Zoology with special reference to Entomology—The Secretary, Birkbeck College, Malet Street, London, W.C.1 (May 11).

Lecturer or Assistant Lecturer in Mathematics at the University College of the West Indies—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (May 15).

Lecturer (preferably with interests in sedimentology or geophysical methods) in Geology at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, May 15).

Assistant Lecturer in Philosophy—The Assistant Registrar, The University, Edmund Street, Birmingham 3 (May 16).

Assistant Lecturer or Lecturer (with a special interest in some aspect of parasitology) in the Department of Agricultural and Forest Zoology—The Secretary and Registrar, University College of North Wales, Bangor (May 16).

Napier Chair of Astronomy—Joint Clerk to the University Court, College Gate, St. Andrews (May 16).

DEMONSTRATOR (with interests in palæontology, stratigraphy, sedimentary petrology or structural geology) IN GEOLOGY—Dr. I. D. Muir, Department of Mineralogy and Petrology, The University, Downing Place, Cambridge (May 23).

WRIGHT-FLEMING CHAIR OF IMMUNOLOGY in St. Mary's Hospital Medical School—The Academic Registrar, University of London, Senate House, London, W.C.1 (May 25).

CHAIR OF PHYSICS in the University of Hong Kong—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Hong Kong, May 30).

CHAIR OF PHARMACOLOGY—The Registrar, The University, Leeds 2 (June 1).

CHAIR OF AGRICULTURE in the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 15).

ASSISTANT FARM MANAGER (with at least a diploma in agriculture), to assist in running a medium-sized mechanized rice farm in Gambia, and to act as Manager when the Farm Manager is on leave—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/12/011.

ASSISTANT LECTURER (Grade B) IN GEOLOGY, to teach up to the standard of the B.Sc. (General) degree—The Clerk to the Governors, Northern Polytechnic, Holloway, London, N.7.

ASSISTANT PROFESSOR OR ASSOCIATE PROFESSOR OF MATHEMATICS—The President, Memorial University of Newfoundland, St. John's, Newfoundland, Canada, and The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1.

GEOLOGISTS (with a degree of a recognized university with either first- or upper second-class honours in geology, two years approved postgraduate experience, and preferably some specialization in mining geology) in the Geological Surveys Department, Federation of Malaya—The Recruitment and Personnel Division, Malaya House, 57 Trafalgar Square, London, W.C.2.

LECTURER (Grade II) IN THE DEPARTMENT OF ORGANIC CHEMISTRY—The Registrar, The University, Bristol 8.

RESEARCH ASSISTANTS (2) (with experience in aeronautical or electronic engineering or in physics) to undertake interesting theoretical and experimental work IN THE DEPARTMENT OF AERONAUTICAL ENGINEERING—The Secretary and Registrar, The University, Southampton.

SCIENTIFIC OFFICER IN THE VIROLOGY DEPARTMENT, for work on plant virus diseases—The Secretary, Scottish Horticultural Research Institute, Mylnefield, Invergowrie, by Dundee.

SENIOR BOTANIST (with a good honours degree in botany and considerable experience in crop breeding, preferably tropical crops) in Tanganyika, for production of improved varieties of crops for irrigation schemes with particular reference to dry season crops, and to lead a team of three breeders—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/8/024.

SENIOR PHYSICS MASTER—The Headmaster, School House, Cranbrook, Kent.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Texas Instruments Limited, Bedford. Semiconductor Application Report, Vol. 1, No. 4: D.C. Power Supply Circuits Using Silicon Rectifiers. Pp. 35. (Bedford: Texas Instruments, Ltd., 1959.) [112

Anti-Locust Bulletin No. 33: Field Observations on the Behaviour of Hoppers of the Red Locust (*Nomadacris septemfasciata* Serville.) By Dr. R. F. Chapman. Pp. ii+51. (London: Anti-Locust Research Centre, 1959.) 9*s.* 6*d.* [122

Ministry of Labour and National Service. Practices Impeding the Full and Efficient Use of Manpower: Report of an Inquiry undertaken by the National Joint Advisory Council. Pp. 16. (London: H.M. Stationery Office, 1959.) 1*s.* net. [122

Bulletin of the British Museum (Natural History). Entomology. Vol. 7, No. 9: A Study of the New Zealand Chironomidae (Diptera, Nematocera). By Paul Freeman. Pp. 393–437+plate 11. 12*s.* 6*d.* Geology. Vol. 3, No. 10: Blue-Green Algae from the Middle Devonian of Rhynie, Aberdeenshire. By W. N. Croft and E. A. George. Pp. 339–353+plates 41–44. 8*s.* (London: British Museum (Natural History), 1959.) [122

International Journal of Radiation Biology and related studies in Physics, Chemistry and Medicine, Vol. 1, No. 1 (January, 1959). Pp. 104. Price per part 20*s.* plus postage. Subscription per volume (4 issues) 75*s.* post free. (London: Taylor and Francis, Ltd., 1959.) [122

Proceedings of the Society for Psychical Research. Vol. 52, Part 188 (February, 1959): Dreaming and Some of Its Implications. By Prof. C. D. Broad. (Presidential Address, 1958.) Pp. 53–78. (London: Society for Psychical Research, 1959.) 2*s.* 6*d.*; 0.50 dollars. [192

University of Leeds. Annual Report of the Librarian, Session 1957–58. Pp. 12. (Leeds: Brotherton Library, The University, 1958.) [192

University of Birmingham: University Research Committee. Twenty-ninth Annual Report (Session 1957–1958). Pp. 108+1 plate. (Birmingham: The University, 1959.) [192

Other Countries

Zweiter Katalog der Astronomischen Gesellschaft für das Aquinoktium 1950. Örter der Sterne bis zur neunten Grösse zwischen dem Nordpol und 2° südlicher Deklination abgeleitet aus photographischen Himmelsaufnahmen der Sternwarten Bergedorf und Bonn, unter Leitung von Richard Schorr und Arnold Kohlschütter. Elfter Band: Deklination +15° bis +20°. Pp. 276. (Bonn: Universitats Sternwarte, 1957.) [102

Metropolitan Life Insurance Company. Statistical Bulletin, Vol. 39, (December, 1958): Large Population Gains in United States and Canada. Fatal Accidents Decrease in 1958. Large Death Toll Under Age 65. Cancer in Childhood. Pp. 12. (New York: Metropolitan Life Insurance Company, 1959.) [122

Western Region of Nigeria. Annual Report on the Forest Administration of the Western Region of Nigeria for the year 1956–57. Pp. iii+34. (Lagos: Government Printer, 1958.) 1*s.* [122

Institut de France—Académie des Sciences. Annuaire pour 1959. Pp. 250. (Paris: Gauthier-Villars, 1959.) [122

An Emerging Program of Secondary School Mathematics. By Max Beberman. (Inglis Lecture in Secondary Education, 1958.) Pp. viii+44. (Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1959.) 7*s.* 6*d.* net. [122

Union of South Africa: Department of Commerce and Industries Division of Fisheries. Twenty-eighth Annual Report for the period 1st April, 1956 to 31st March, 1957. Pp. 160. (Reprint from *Commerce and Industry*, September, 1958.) (Pretoria: Government Printer, 1958.) [122

Commonwealth Scientific and Industrial Research Organization, Australia. Soil Publication No. 12: The Characteristics and Origins of Soils in the Coleraine District, Victoria. By G. Blackburn and T. I. Leslie. Pp. 47+1 map. (Melbourne: Commonwealth Scientific and Industrial Research Organization, 1958.) [182

East Africa High Commission. East African Industrial Research Organization Annual Report, 1957–1958. Pp. ii+18. (Nairobi: Government Printer, 1958.) Sh.2. [182

Annals of the New York Academy of Sciences. Vol. 75, Article 2: The Uterus. By Joseph T. Velardo, William B. Ober, Herbert G. Winston and 72 other authors. Pp. 385–1040. (New York: New York Academy of Sciences, 1959.) 7 dollars. [182

Indian Forest Records (New Series). Entomology. Vol. 9, No. 6: Some More Indian Geomatrid Larvae (Lepidoptera), with a Note on the Identity of Components of Various Groups of Setae. By Balwant Singh. Pp. ii+131–163+1 plate. (Delhi: Manager of Publications, 1957.) Rs. 1.50; 2*s.* 3*d.* [182

Proceedings of the Third Congress on Theoretical and Applied Mechanics, Bangalore, December 24–27, 1957. Pp. xi+362. (Kharagpur: Indian Society of Theoretical and Applied Mechanics, Indian Institute of Technology, 1958.) n.p. [182

Geological Society of South Africa. New Observations on the Ores of the Witwatersrand in South Africa and their Genetic Significance. By Prof. Paul Ramdohr. Pp. 50+61 plates. (Annexure to Vol. 61 of the *Transactions and Proceedings of the Geological Society of South Africa.*) (Johannesburg: Geological Society of South Africa, 1958.) [182

Research Bulletin of the Panjab University. No. 131 (Zoology): A Histological Study of the Brain, Optic Lobes and Thoracic Nerve Cord of *Petrobius brevistylis*, with special reference to the Descending Nervous Pathways. By R. C. Satija. Pp. 493–510+7 plates. Rs. 3/50. No. 132 (Zoology): Studies on the Course and Functions of the Giant Nerve Fibres from the Eye and the Tegumentary Nerve to the Central Nervous Cord in *Locusta migratoria*. By R. C. Satija. Pp. 511–519+2 plates. Rs. 1/75. No. 133 (Zoology): Cytological Studies in Heteroptera. 4: Chromosome Complement and Meiosis in Twenty-six Species of the Pentatomoidea, Lygaeoidea and Coreoidea, with a Consideration of the Cytological Bearing on the Status of these Super-Families. By Ram Parshad. Pp. 521–559. Rs. 5/23. No. 134 (Zoology): A New Genus of the Spiders of the Family Sparassidae. By Sukh Dyal. Pp. 561–566+1 plate. Rs. 1/36. No. 135 (Chemistry): Studies in Surface Chemical Reactivity and Surface Area of Suspensoids. Part 1: Methods of Estimation. By Balwant Rai Puri, J. Singh, D. D. Singh and Lekh Raj Sharma. Pp. 1–7. Rs. 1/32. No. 136 (Chemistry): Studies in Surface Chemical Reactivity and Surface Area of Suspensoids. Part 2: Relationship between Surface Reactivity and Surface Area of a Few Oxide Gels. By Balwant Rai Puri, H. Singh, D. D. Singh and Lekh Raj Sharma. Pp. 9–12. Rs. 0/89. (Hoshiarpur: Panjab University, 1957 and 1958.) [182

Research Bulletin of the Panjab University. No. 137 (Zoology): A Histological and Experimental Study of Nervous Pathways in the Brain and Thoracic Nerve Cord of *Locusta migratoria migratoriodes* (R. & F.) By R. C. Satija. Pp. 13–32+8 plates. Rs. 3/85. No. 138 (Zoology): A Histological Study of the Brain and Thoracic Nerve Cord of *Aeshna* Nymph with special reference to the Descending Nervous Pathways. By R. C. Satija. Pp. 33–47+7 plates. Rs. 3/10. No. 139 (Zoology): A Histological Study of the Brain and Thoracic Nerve Cord of *Apis mellifera* with special reference to the Descending Nervous Pathways. By R. C. Satija. Pp. 49–65+9 plates. Rs. 3/60. No. 140 (Zoology): On a New Species *Ceylonocotyle dawesi* from *Bosindicus* Linn., in Madras (South India). By N. K. Gupta. Pp. 67–73. Rs. 1/40. No. 141 (Zoology): On Two New Trematodes of Bats, *Lyroderma Lyra* (Geoffroy) in Gurdaspur, India. By N. K. Gupta and O. N. Bhardwaj. Pp. 75–79. Rs. 1/10. No. 142 (Zoology): A Histological Study of the Brain and Thoracic Nerve Cord of *Callophora erythrocephala* with special reference to the Descending Nervous Pathways. By R. C. Satija. Pp. 81–96+6 plates. Rs. 3/28. No. 143 (Zoology): Histochemical Studies of Protozoa. 1: Studies on the Lipids in *Opalina ranarum* and *O. scalpriformis*. By G. P. Dutta. Pp. 97–106. Rs. 1/65. (Hoshiarpur: Panjab University, 1958.) [182

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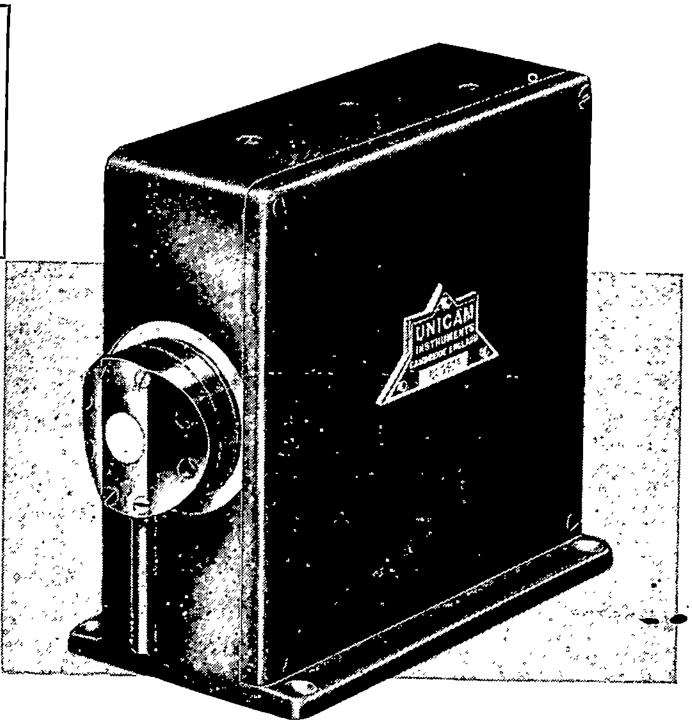

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U 165

THE RELATION OF EDUCATION TO RESEARCH

IN opening a debate on education in the House of Commons on January 22, the Minister of Education, Mr. Geoffrey Lloyd, stressed the need for maintaining a balance between the different steps on the educational ladder. He said little about the grammar schools, apart from a passing tribute to the way they had adapted themselves to the scientific age. The secondary modern schools had no long traditions to help them, but Mr. Lloyd said that in spite of handicaps some of them had considerable achievements to their credit, and 75 per cent of all children in some schools remained on after the compulsory age. Referring to the supply of teachers, Mr. Lloyd said that he hoped to make the training colleges much more like university institutions than many of them had been in the past, and that if it was clear that the 50 per cent expansion proposed by the Government was not enough, the Government would re-consider the expansion programme. There was no reference specifically to science teaching, but it has been stated that £2 million a year is being spent on laboratory buildings at maintained secondary schools, though without much more help the position at this critical point may well deteriorate rather than improve, as Dr. K. Hutton's recent address at the North of England Education Conference indicated.

In replying on the debate, the Parliamentary Secretary to the Ministry of Education, Sir Edward Boyle, pointed out that while the number of children in primary schools had fallen by 150,000–200,000 in the past two years, 200,000 extra places have been provided. Primary schools themselves will benefit in three ways from the Government's proposals for secondary education. Removal of senior children from all-age schools will leave more space for the younger children; resources are to be found during the five-year period both for building new primary schools in new housing areas and for completely replacing some of the worst primary school buildings; and a substantial part of the resources available for minor projects (costing less than £20,000) will be devoted to improving primary schools. As regards the reduction of all classes, junior and senior, to a maximum of thirty, Sir Edward Boyle pointed out that this would require a further 110,000 teachers over and above the present 260,000, and an increase of this scale is impracticable during the next few years. Finally, he repeated the assurance in the White Paper that there would be no attempt at a uniform pattern of secondary education. Whatever the best solution may be in new housing areas or sparsely populated areas, in Mr. Lloyd's view it would be wrong so to organize secondary education in the big cities of Britain as to leave parents no freedom of choice and to uproot good established schools, especially grammar schools, which are already doing first-class work.

Almost the only reference to expenditure in the debate was that of Mr. J. C. Jennings, who pointed out that the Government is already committed to £300 million for school building in the next five years, to £15 million for training colleges, £100 million for technological education and to £95 million between 1957 and 1963 for universities, and it is expected that the total figure of approaching £800 million for the present year would reach £1,000 million by 1963–65. Since then, the Minister of Education has given further details of the training college programme, which will include about seventy projects and is inspired by five principles: a considerable increase in the average size of the colleges, so that 40 per cent will have more than 400 places and provide 60 per cent of the total intake; the colleges will be made much more like university institutions than in the past; there will be a sensible distribution of the new places throughout England and Wales, with particular attention to areas with a serious shortage of teachers; special emphasis is being given to the training of more teachers of science and mathematics, and of certain other practical subjects; and the number of colleges catering for both men and women will be more than doubled.

The prospective supply of staff was one factor which has led the Minister to limit the current programme to 12,000 places, but Mr. Lloyd has already told the House of Commons that he is prepared to extend the programme if it appears that this 50 per cent expansion is insufficient, though he indicated that it would probably be wiser to extend the programme for a year or two after 1962 than to attempt more before then. On February 9 the Chancellor of the Exchequer announced that he proposed to ask Parliament to increase by £2,550,000 the recurrent grant of £34,350,000 already proposed for the universities for 1959–60, and to increase those for 1960–61 (£36,750,000) and 1961–62 (£39,500,000) by £2,660,000 and £2,720,000, respectively. The Department of Scientific and Industrial Research, moreover, is now prepared occasionally to recommend grants for special researches for periods up to seven years initially, instead of five years, as hitherto, and its new policy may well tend to increase the total allocations to the universities, even if the actual awards are earmarked for research. Furthermore, some of the evidence submitted to the Anderson Committee on Grants to Students, notably the recommendations from the National Union of Students that awards should be made without reference to parental income, would, if accepted, further increase the national expenditure on university education by perhaps £1·5 million a year.

Apart from its failure to consider expenditure and the critical issue of science teaching, the debate was disappointing in that secondary education was not properly considered either in relation to the educational system of Britain as a whole or, apart from the stress laid by both Ministers on the need to consider the individual boy or girl, to the demand for talent. It should be almost a corollary of providing equality of opportunity and freedom for the gifted individual student to develop his or her ability to the full that there should be some relation between the scale of public education and the opportunities which the nation can provide for trained man-power. Notably the debate was characterized by lack of appreciation of the interdependence of the various levels of education, and of the way in which expenditure at one stage might limit expenditure at others, quite apart from considerations of available teachers or other resources.

Such considerations should determine Britain's expenditure on university and technical education, and the form which university expansion should take. Dr. B. V. Bowden has urged that we need more and bigger schools and more and bigger universities if we are to develop higher education sufficiently to meet Britain's needs as a great manufacturing and trading country. He has pointed out, too, that industry has a large part to play in developing and financing this expansion, and that unless industry prepares now, the larger number of graduates in technology and engineering who will be leaving the universities and colleges of technology in a few years time will be unable to complete their education. Moreover, such co-operation is not entirely one-sided. In Dr. Bowden's view, British universities do not make sufficient use of the facilities for research which are available in industry or through the Department of Scientific and Industrial Research.

This is a particular aspect of the organization in Britain for research, and it is one to which due attention should be paid in considering the functions of that Department's own research stations and of the research associations. There are dangers in the isolation of such institutions from academic life, as there are in the isolation of the universities themselves; and the repercussions between research and teaching are also complex and merit more attention. Apart from the question whether students in general should be encouraged to take up research unless they contemplate such a career and evince aptitude for research, there are questions as to the bearing of research on effective teaching, particularly in relation to facilities and the technical assistance available to the teacher who is also occupied in research.

All this is related, too, to the question of the size and distribution of universities in Britain as well as their number. The discussion on the size of universities and university departments at the Conference of the Universities of the United Kingdom last December showed that we are as yet far from agreement as to the right solution of the problem of university expansion. Sir Patrick Linstead argued cogently that it is important at such a time of rapid expansion to consolidate existing institutions rather than found new ones, and the argument that proper weight must be given to the efficient size of departments and of faculties has the more force when it is essential to ensure the maximum use of available resources in finance and in teaching staff. Sir Patrick considers that a university department in subjects which are rapidly expanding and sub-dividing should have at least 150–200 students, and while he does not favour expansion of non-collegiate universities beyond about 4,500 students, he thinks that an arts faculty should contain at least 1,000, a science faculty 600 and a faculty of applied science 800 students.

Sir Patrick believes that the principles he puts forward, if applied to the existing universities of Britain, including the projected University of Sussex, would provide sufficient space for all but 5,000 of 124,000 students visualized by 1965, and that this deficiency could be met by founding one new university, for example, at Norwich, and developing three or four new faculties of technology at existing universities. Prof. E. Devons thinks that the problem of size requires rather more study, and like Lord Simon in a recent article in the *Universities Quarterly*, leans towards a comparative study of university administration and organization, without, however, suggesting that a Royal Commission is needed. Lord Simon, it is true, suggested that numerous other problems, such as the factors determining university expansion, the allocation and control of grants by the University Grants Committee, the abolition of fees, the relations between research and teaching, merit independent examination.

Dr. R. Pedley, however, at the Universities Conference, favoured the establishment of several new universities largely because of the unequal contribution which a university can make to the quality of regional culture, and for this reason visualized new universities on Teeside, in mid-Lancashire, Coventry and the Home Counties. He also thinks that a further 46,000 places will be required by 1965, even if only 5 per cent of the pupils in comprehensive schools qualify for university entrance. He does not believe, moreover, that a scarcity of university teachers of high calibre is a sufficient reason for denying university education to those who might profit by it, and, while urging the desirability of a graduate teaching profession, he is prepared to accept a higher ratio of students to staff until 1970 than at present, provided those students had learned in school how to study and how to organize their lives.

As might have been expected, the Universities Conference showed awareness of the need for the educational system to be balanced; but that is very far from being fully recognized by Parliament as yet, nor has the Government taken any apparent steps to secure such a balance, even within whatever limits of expenditure it is prepared to propose. The Earl of Dundee, in replying for the Government on a notable debate on the youth services in the House of Lords on February 4, did indeed stress the importance of the contribution which the varied institutions of further education, including many voluntary bodies, have to make to the preservation of the permanent values in human character on which the stability of our way of life so largely depends. Unless such virtues as discipline and unselfishness, patriotism and loyalty and true religion are actively fostered, the best literary and scientific education in the world will not preserve the soul of a great country, and scientific progress and material achievement may come to naught.

The problems of educational expansion are indeed complex and varied, but it is not difficult to discern the correct priorities at any moment, though those priorities will themselves change from time to time. What is of first importance at present is that policy should be determined not by political doctrine but by educational needs and experience. There is indeed much that is common ground between the major political parties, and ample room for experiment without disturbing the functioning of existing institutions by introducing political uncertainty. An all-party approach would likewise assist to make available the greater resources Britain clearly needs to allocate to education, and to secure the most effective distribution of those resources. The task at any level is too immense for us to look for success except by co-operation on a much greater scale than in the past, and to promote the appropriate atmosphere of co-operation is a first duty of every responsible citizen. In such an atmosphere it will be the easier to resolve wisely the inevitable clashes between sectional and national views, and to secure the agreement to allocate special effort or resources at whatever point, such as the training of teachers of science, the improvement of school laboratories, or the expansion of technical colleges, that may at the moment be most needed, or to take the less spectacular measures designed to avoid waste of talent and resources and ensure that the country gets full value from its mounting expenditure on education.

SOCIAL POLICIES AND SOCIAL CHANGE

Essays on 'The Welfare State'

By Prof. Richard M. Titmuss. Pp. 232. (London: George Allen and Unwin, Ltd., 1958.) 20*s*. net.

In the course of the first of this series of essays Prof. R. M. Titmuss comments that it was characteristic of Prof. R. H. Tawney that he constantly reminded his students that "the most important thing about a man is what he takes for granted". It is equally characteristic of Prof. Titmuss that he makes it impossible for his readers to go on taking for granted those presuppositions about social policies and institutions which are all too easily accepted and acted upon by so many people. Whether he is writing about the differing provisions made for income maintenance in old age, about the position of women in modern society, about medical care under the National Health Service, he is careful to examine the relevant data afresh, often bringing to light new or little-known information in the process. The resultant discussions are always stimulating and illuminating. Sometimes they are disconcertingly so, and whether we accept his final conclusions or no, Prof. Titmuss certainly challenges us to think again about the subjects under discussion.

The topics covered in this collection of essays are varied and at first sight disparate, but, as is pointed out on the fly-leaf, two broad themes unite them—changes in social structure and developments in social policy, and it is one of the chief merits of Prof. Titmuss's whole approach that he relates the two processes in a way seldom attempted either by academic sociologists or students and practitioners of social administration. For example, pension policies are considered in the context of population change, and current problems and practices of the National Health Service are related both to the scientific revolution in medicine which began in the late 1930's and to the psychological and social factors affecting the individual's and society's attitude towards health, disease and medical care. The relationship between institutions and policies is similarly emphasized in those essays which take as their starting point a social institution. For example, in the essay on "Industrialization and the Family", Prof. Titmuss shows that, on one hand, problems of human relations in industry cannot be solved within industry itself, and on the other, that the family does not function in a social vacuum. Rather is it profoundly affected by the forces of industrialization, and in this context we can see the social services in "a variety of stabilizing, preventive and protective roles".

Not only do these essays differ in subject-matter, they are based on lectures given at different times and places to audiences of different background and outlook. The first was delivered in 1951 at the London School of Economics, whereas those on the National Health Service were addressed to an American audience at Yale in 1957. This does not destroy the underlying unity, but it does mean that each essay is more or less self-contained, and the book as a whole, valuable and stimulating as it is, is but a foreshadowing of what Prof. Titmuss might achieve had he the leisure and opportunity to produce a major work dealing with the broader aspects of social policy, to the study of which he brings such depth of insight and breadth of vision. M. P. Hall

THE QUINTESSENCE OF PARACELSUS

Paracelsus

An Introduction to Philosophical Medicine in the Era of the Renaissance. By Walter Pagel. Pp. xii+368. (Basel and New York: S. Karger, 1958.) 70 Swiss francs.

Probably no other figure in the history of medicine and science offers greater difficulties to our understanding than Paracelsus. Probably none of the numerous books on Paracelsus is more helpful in forming an objective and clear appreciation of Paracelsus than this new book by Dr. Pagel.

The author achieves this goal by concentrating on the philosophy of Paracelsus, which sees cosmology, theology, natural philosophy and medicine in the light of analogies and correspondences between the macrocosm and the microcosm, man. Naturalism is with Paracelsus the search for divine signs. He is, therefore, with all his protoscientific ideas and achievements, not a scientist in the modern sense.

The author analyses in detail the Paracelsian concepts of 'experience', astrology, time, the elements, the famous three principles (sulphur, salt, mercury) and quintessence. There is a certain contradiction between the microcosmic dilution of man and the idea of specificity, equally important to Paracelsus, and embodied in the archeus or archei. 'Imagination' provides man with great spiritual power.

The medicine of Paracelsus is but an application of these general ideas. Paracelsus regarded diseases as specific fruits of the human body in the same fashion in which the metals were specific fruits of the earth. In spite of his chemical pathology Paracelsus tends toward localizing disease on his firmament of organs. But disease is essentially the result of an extraneous force, an invader, a seed. This specific agent has to be treated etiologically by specific remedies (ancient therapy was non-specific), which are often chemicals. Paracelsus paid particular attention to diseases due to tartar, fought the doctrine of catarrh, and developed a new theory of plague. He began to replace medieval uroscopy by quantitative and chemical analysis of urine. The author gives a long list of his practical achievements in medicine, always combined with wild speculations (antiseptic principles, syphilis, mercury as a diuretic, hydrotelluric theory of goitre, balneology, miners' diseases).

Dr. Pagel then analyses with wonderful scholarship and great penetration the sources of Paracelsus: gnosticism, the Cabbala, neoplatonism, Avicebron, Ramon, Lull, Arnuld of Villanova, the alchemists John de Rupescissa, Reuchlin, and Agrippa of Nettesheym. He also discusses in detail Paracelsus's great critic, Erastus, and his moderate defender, Daniel Sennert.

Paracelsus was, according to the author, an able chemist, and his medicine has elements of what was to become modern medicine. But his chemistry and his medicine were but parts of his symbolistic, decidedly unscientific cosmology and philosophy. He produced scientific results from a non-scientific world of motives and thoughts. He offered little which in principle cannot be found with his medieval predecessors, but he integrated all these elements into a new doctrine of medicine and natural philosophy. Without Paracelsus there would have been no iatrochemistry. He was a 'Magus' who forged a new synthesis from personal experience.

I do not hesitate to rate this book as the most valuable in the whole extensive literature on Paracelsus from the point of documentation as well as judgment. It is a high point in the author's long and distinguished career as a medical historian, which began with his work on van Helmont in the late 1920's and continued the great accomplishments of his father, Julius Pagel. It avoids equally the nebulous enthusiasm and the embittered hostility encountered so often in writings on Paracelsus. Dr. Pagel unites an unqualified attachment to modern science with a profound feeling for and understanding of mystic and magic philosophy. This rare combination enables him to be just and to give us the quintessence of Paracelsus.

Erwin H. Ackerknecht

MEDICINE IN INDUSTRY

Industrial Hygiene and Toxicology

Edited by Frank A. Patty. Vol. 1: General Principles. Second, revised edition. Pp. xxvii+830. (New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1958.) 17.50 dollars.

The first edition of Patty's "Industrial Hygiene and Toxicology" was published in 1948 in two volumes. The second edition is to be in three volumes, of which the first is now ready. It is not possible to assess the whole work until it finally appears, but, according to the preface to the second edition, much of the new matter has been placed in the first volume. The main changes are to be found in the treatment of such subjects as noise, heat, ionizing radiations, human engineering and industrial safety, sanitation, air pollution and illumination. Additional chapters on air conditioning, air cleaning, and heat control in the hot industries are included, as well as separate chapters on illumination and industrial sanitation. Dr. O. A. Sander contributes a revised chapter on the pulmonary dust diseases, Dr. L. Schwartz and Dr. Carey McCord bring up to date their chapters on the industrial dermatoses and the visible marks of occupation, respectively. The editor, Mr. Frank Patty, is responsible for four chapters on such subjects as the industrial hygiene survey, the mode of entry and action of toxic materials and sampling and analysis of atmospheric contaminants, in addition to his introductory chapter on industrial hygiene. This chapter calls for some comment, because Mr. Patty seems to have the idea that analyses of the contaminants of factory atmospheres did not begin in Great Britain until the formation of the Occupational Hygiene Society in April 1953, and that until that date medical control and not engineering control of health risks had been used. The fact is that both methods of control have been used in Great Britain for many years. Nevertheless, industrial or occupational hygiene is a rapidly developing subject, and the industrial health engineer is a new importation from the United States.

The first edition of Mr. Patty's book was an ambitious, but rather uneven, attempt to bring all the facets of industrial hygiene within the same close and curtilage. It showed that the industrial health engineer has the freedom of engineering, chemistry, physics, biology, physiology and medicine, and speaks with equal authority on all of them. In this age of super-specialization, the health engineer is therefore a refreshing phenomenon. The engineer who writes with authority on clinical medicine and hæmatology, without the benefit of a medical training, is to be congratulated on his courage. No doctor with experience of industry has yet been bold enough to write and edit a book on engineering. But that state of affairs may yet arise, because the industrial doctor in Britain is obliged to make himself familiar with the intimate details of factory processes, and with the estimations of contaminants in the atmosphere and its engineering control. In the United States it is rare for the plant doctor to deal with such matters, which are left to the health engineer, or industrial hygienist. It seems to us in Britain that the American version of the health engineer is probably taking on too much responsibility for health matters. No doubt in the course of time the industrial hygienist will find his proper place. Mr. Patty himself shows that the position in the States is being slowly modified. "Industrial hygiene," he writes, "has successfully withstood abortive efforts at absorption by both safety engineering and medicine. It borders on each of those fields, but differs in technique from both, and one of its primary functions is to get these two groups to work hand in hand." He has little doubt that regular and more frequent medical examinations are a desirable way of discovering dangerous exposures, especially in the absence of competent industrial hygiene engineering and control; and he affirms that when the two methods are properly co-ordinated, the most dependable safeguard against harmful exposures is provided. He has yet to reach the logical conclusion that the major responsibility for health matters in industry rests with the medical profession, assisted, as it should be, by capable and knowledgeable industrial hygienists.

A. I. G. McLaughlin

RADIOACTIVE ISOTOPES IN BIOCHEMISTRY

Radioaktive Isotope in der Biochemie

Von Prof. Engelbert Broda. (Einzeldarstellungen aus dem Gesamtgebiet der Biochemie, Neue Folge, Band 3.) Pp. viii+326. (Wien: Verlag Franz Deuticke, 1958.) 294 schillings.

FEW techniques have had a more widespread or profound influence on modern biochemistry than the application of isotopes. Although the first experiments were carried out by Hevesy more than thirty-five years ago, many isotopes have been available for a much shorter time and the use of isotopes in biochemical research has increased remarkably in the past fifteen years, as shown in an instructive table in this book. During the same period there have been considerable improvements in the instruments required for radioactive tracer work and there is thus sufficient scope for a new book, despite the existence of several well-established works.

Prof. E. Broda of the University of Vienna has written a book which is intended to serve both as an introduction to the methods used in work with radioactive isotopes and as an outline of the major biochemical problems in which isotopes have been particularly useful. Thus, the first eight chapters of the book deal with the production of isotopes, the synthesis and biosynthesis of labelled compounds, the hazards involved in work with radioactive substances, precautionary and protective measures, and the measurement of radioactivity. The treatment is concise, easily intelligible and useful for those interested mainly in acquiring sufficient knowledge for applying radioisotopes to their own problems.

The next two chapters deal with analytical applications, such as the isotope dilution method, and with metabolic pools and turnover. Finally, there are five chapters on main problems (phosphorylation, photosynthesis, carbon dioxide fixation, the metabolism of carbohydrate, fat, protein and nucleic acids, the citric acid cycle, purine and pyrimidine biosynthesis) and one on special problems of metabolism (immunological problems, the biosynthesis of porphyrins, cholesterol and lignin). This last chapter also contains a very brief (five pages) and somewhat inadequate section on the metabolism of biologically active compounds such as vitamins, drugs and carcinogens.

Although the book has been deliberately restricted to radioactive isotopes, stable isotopes are fortunately not completely neglected. For example, double intramolecular labelling with deuterium and carbon-14 is briefly mentioned (p. 31) and the importance of the stable isotope nitrogen-15 is indicated on pp. 223–29. The only notable omission is the application of isotopes, both stable and radioactive, to studies of the mechanism of enzymic reactions.

The book is well produced and there are very few errors. In some cases, however, there are slightly misleading statements, as for example on p. 16 where it is suggested that oxygen exchanges between the two positions of a carboxyl group, which are, of course, equivalent because of the symmetry of the carboxylic anion. It is a little surprising to read that the basic outline of protein synthesis is still completely unknown (p. 216) and that carboxyl activation of amino-acids is regarded as merely probable (p. 221). Also on p. 221 there is some confusion between transpeptidation and *de novo* peptide bond synthesis. But these are perhaps only minor matters in a book primarily concerned with isotopes.

The literature references are remarkably up to date, many of them being to publications which appeared in 1957. It is to be hoped that an English translation of this useful book will be forthcoming.

H. R. V. ARNSTEIN

NUCLEAR ENGINEERING MONOGRAPHS

Nuclear Engineering Monographs

No. 1, Elementary Nuclear Physics. By W. K. Mansfield. Pp. viii+60. 10*s*. 6*d*. net. No. 2, Nuclear Reactor Theory. By J. J. Syrett. Pp. viii+80. 12*s*. 6*d*. net. No. 3, Reactor Heat Transfer. By W. B. Hall. Pp. viii+68. 10*s*. 6*d*. net. No. 4, Nuclear Reactor Shielding. By J. R. Harrison. Pp. viii+68. 10*s*. 6*d*. net. No. 5, Nuclear Reactor Control and Instrumentation. By J. H. Bowen and E. F. O. Masters. Pp. x+78. 12*s*. 6*d*. net. No. 6, Steam Cycles for Nuclear Power Plant. By W. R. Wootton. Pp. vii+66. 10*s*. 6*d*. net. (London: Temple Press, Ltd., 1958.)

THE first three books in this excellent series were published about a year ago, and the final three quite recently. The six fall into two classes: Nos. 1, 2 and 4 provide summaries of matter which is readily available in greater detail elsewhere; and Nos. 3, 5 and 6 provide summaries of matter either not previously published or else dispersed rather widely.

There is general agreement that nuclear engineering is more appropriately studied at postgraduate level. However, nuclear physics is a useful subject for inclusion in the final year of undergraduate syllabuses and many universities provide this type of course. Advanced physics text-books are inappropriate at this stage, but the first monograph dealing with the modern concept of the atom, radioactivity, nuclear reactions and the detection of nuclear radiations is at a suitable level.

A physicist or engineer dealing in great detail with reactor physics might prefer to by-pass the monograph on reactor theory and work directly on the more comprehensive standard texts. The design of a reactor core is essentially a compromise of many conflicting criteria and a large number of engineering designers need to know the form in which the physicist does his calculations and the probable significance of changes in core geometry. Mr. Syrett's concisely written book outlines the framework of this important subject, and the text is sufficiently brief to assist in absorbing the principles. Even when reading the more detailed text-books it is useful to have the monograph to hand to show the way through what might otherwise appear a very complex analysis. The monograph deals with the slowing down and diffusion of neutrons, lattice calculations and the calculation of critical size. The chapter on "Reactor Operation at Power" is a particularly good introduction to the subject.

The third monograph in the first class mentioned above is that on reactor shielding. The author introduces his book by saying that a great deal of experimental and theoretical work is being undertaken on the subject of shielding and that 'art' is being replaced by science. Existing texts on the subject are bulky and contain masses of data. The monograph is welcomed as providing a guide to the important considerations; it is divided into three main sections, the first dealing with gamma-rays and their attenuation, the second with the neutron physics relevant to shield design, and the third with practical shield design.

The first monograph in the second group is that on heat transfer. Little had been published on reactor core heat transfer in Britain prior to the 1958 Geneva conference. This book is divided into two sections, and most experimenters will be sympathetic in the method of splitting as between fundamental work and work of immediate practical application. The heat-transfer specialist in nuclear power has the twin function of testing fuel-element cans under simulated reactor conditions to give exact design figures, and of carrying out inspired research work to provide the answers for subsequent stages in reactor development. The chapter on fundamentals sets out in a concise form the analytical approach, and describes the various analogies between heat and momentum transfer. The second chapter derives the usual design formulæ for channel heat transfer and pressure drop and ends with a comparison of gaseous coolants and a worked example. The final chapter considers such topics as liquid-metal heat transfer, fin efficiency and a comparison between liquid and gaseous coolants.

The monograph on reactor control and instrumentation is welcomed as providing a basis for later, more detailed, texts on these subjects. The incident at Windscale emphasized the need for comprehensive instrumentation in present reactor designs, and the lecture by Sir John Cockcroft in Tokyo last November mentioned two phenomena, positive moderator temperature coefficient and disturbances in the power distribution in a reactor due to local changes in xenon poisoning, with which the designers of the current stations have to cope. The present monograph must suffice until nearer the commissioning times of the Central Electricity Generating Board and the South of Scotland Electricity Board stations. The subject of control is a complex one ranging from neutron kinetics to the thermal response of a steam-raising unit. The monograph deals with neutron kinetics conventionally. The following chapter on temperature-stabilized reactors is important. As the authors mention, this type of analysis would in practice be carried out using an analogue computor. The numerical and graphical methods described do, however, show the trends. In later editions of these monographs, the final chapter of this book on instrumentation might well prove the basis for a seventh monograph, and then include health physics instrumentation.

The monograph on steam cycles consists of two main sections, one dealing with graphite-moderated, gas-cooled reactors, and the other with water-cooled, water-moderated reactors. It is worth remembering that the dual pressure cycle for the former type of reactor was first suggested in 1948. Since that time considerable effort has been expended in dealing with the number of variables involved. The essential tools are given in the appendixes, but the work involved is laborious. It is to be regretted that some co-operative effort was not made years ago to publish comprehensive graphs of the form given in this book. The section on water-cooled reactors deals with both pressurized-water and boiling-water types, and includes a short section on the use of a coal-, oil- or gas-fired superheater.

The editor of this series is to be congratulated in providing a number of stimulating monographs.

R. Vaux

LOW TEMPERATURES

Low Temperature Physics and Chemistry

Proceedings of the Fifth International Conference on Low Temperature Physics and Chemistry held at the University of Wisconsin, Madison, Wisconsin, August 26–31, 1957. Edited by Joseph R. Dillinger. Pp. xxv + 676. (Madison, Wis.: University of Wisconsin Press, 1958.) 6 dollars.

Kältetechnik

Von Prof. Matts Bäckström. Zweite überarbeitete Auflage. Bearbeitet und ins Deutsche übertragen von Dr.-Ing. Eduard Emblik. Pp. xvi + 656. (Karlsruhe: Verlag G. Braun; London: K. G. Heyden and Co., Ltd., 1957.) 56 D.M.; 98*s*.

INTERNATIONAL conferences on the progress of low-temperature physics are held bi-annually. The book, published by the University of Wisconsin Press and edited by Dr. J. R. Dillinger, contains the reports of such a conference held in Madison, Wisconsin, in 1957. The reports were furnished by the speakers and, since it was originally intended to bring out a simple stencilled version quickly, the figures are in many cases rough diagrams. Altogether, more than two hundred reports from all branches of low-temperature research are presented, and it is, of course, ~~quite~~ impossible to give even a rough survey of the contents.

The previous low-temperature conference was held in Paris in 1955 and much of the work reported in Wisconsin is necessarily a continuation of research discussed at the Paris meeting. There were a number of new developments in the field of nuclear orientation. The most outstanding of these are the experiments on the anisotropy of beta emission which provided the proof of the non-conservation of parity postulated by Yang and Lee. Another paper reported the successful orientation of nuclei by the method suggested by Pound in which use is made of the coupling between the lattice electric field and the nuclear quadrupole moment. It is unfortunate that a special lecture by Dr. N. Kurti on nuclear cooling has been published separately and is not included in the book.

An important advance in the theory of superconductivity was made by Bardeen, Cooper and Schrieffer, and a number of papers were read on experimental confirmations of this work. In particular the work on absorption of radiation at wavelengths between 0·1 and 1 mm. and that on the change of ultrasonic attenuation when a metal becomes superconductive deserve mention. The first reports were also submitted on a practical application of superconductivity which may lead to far-reaching developments. This is the use of superconductive switching elements in computors and in memory devices.

A certain amount of new information on liquid helium and especially on the behaviour of the light isotope is noted. Interesting advances have been made in the cryogenic use of the latter and it was regretted that Soviet scientists, who have done much work in this field, had not been able to attend.

Dr. Bäckström's book is a translation into German of the Swedish original. It deals with a great many aspects of refrigeration technique, mainly in the range of interest for food storage. It is not a text-book but rather an information manual which will be of interest to those specializing in this field.

K. Mendelssohn

The Measurement of Soil Properties in the Triaxial Test

By Dr. Alan W. Bishop and D. J. Henkel. Pp. viii+190. (London: Edward Arnold (Publishers), Ltd., 1957.) 70*s*. net.

THE Department of Soil Mechanics in the Imperial College of Science and Technology, London, has a standing in teaching and research second to none among schools of soil mechanics, and its students are drawn from all over the world. This is at once an assurance that the training given is valued and widely disseminated. Dr. A. W. Bishop is reader and Mr. D. J. Henkel lecturer in this Department, and to read their book is to be taken with firm direction through a course of instruction in their own laboratory; to be taught sufficient about the application of triaxial tests to appreciate their significance, and much of the art of making the tests and keeping them meaningful. The authors tell us they do not intend their book as a manual, presumably because they have limited themselves to describing the methods and theories which have been developed at the Imperial College, but though it may not be a manual, there is no doubt that for many readers it will form an adequate text-book. Its four parts deal with the [redacted] application of test data; the detailed construction of apparatus; the standard tests for which the apparatus is intended, and various special tests for which it may be used.

The ground is covered thoroughly, and where points of theory or application are not presented, the relevant references to the literature are given. Particularly welcome are the sections concerning the determination of the pore pressure parameters *A* and *B*, which form the basis of the concept of shear strength introduced by Skempton and Bishop in 1954. The book is well produced and contains many diagrams, detailed drawings and photographs of apparatus. Soil-mechanics engineers will welcome it as a work of reference, but its price will cause a student to debate the need for adding it to his own bookshelf.

THOMAS WHITAKER

Clinical Hæmatology in Medical Practice

By G. C. de Gruchy. Pp. xii+620. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, 1958.) 50*s*. net.

IN the best organized institutions the physician and hæmatologist work in close collaboration. The hæmatologist must know enough about the clinical state of the patient to know which tests are appropriate, and the physician must know enough about hæmatology to be able to interpret the results. Dr. de Gruchy's book provides just this information. It gives an accurate balanced account of hæmatological disorders with enough clinical details to enlighten the hæmatologist and enough about the interpretation of technique for the physician. It would be very easy for such a book to become unwieldy, but Dr. de Gruchy has avoided this by the total omission of technical detail and the free use of tabulation. The presentation is somewhat dogmatic and it is this which makes the book so easy to read. But, of course, it is never possible to be dogmatic and agree with all workers on every subject. For example, it is probable that workers with experience in the surgical treatment of hæmophilic patients would not consider that a transfusion of 20 ml. of fresh plasma per kgm. body-weight would be likely to control bleeding. However, such details are really irrelevant; anyone wishing to undertake some very specialized treatment would naturally consult original papers on the subject and would not rely exclusively on a book, the main object of which is the general education of physicians and clinical pathologists.

R. BIGGS

Clinical Enzymology

Edited by Dr. Gustav J. Martin. Pp. vii+241. (London: J. and A. Churchill, Ltd., 1958.) 42*s*. net.

ALTHOUGH clinical enzymology is not a new sphere of activity in medical science it is a subject that has been greatly fostered by the purification and crystallization of enzymes during recent years. From this has come a realization that enzymes can be usefully administered parenterally in many instances. This book begins with a discussion of protein biology and the chemistry and biochemistry of enzymes which are of clinical value. The diagnostic use and the therapeutic action of enzymes are also considered and the book concludes with a discussion of future possibilities. The parenteral administration of trypsin in particular has been of value in the treatment of conditions involving intravascular clotting, in the treatment of infected wounds, and in a wide range of infections generally. On the whole, the anti-inflammatory action of the enzyme is the most striking. Other enzymes which have been used parenterally include streptokinase, deoxyribonuclease, hyaluronidase, and cholinesterase, but for the value of the use of most of these by parenteral administration only fragmentary evidence exists. It can be said without hesitation, however, that the medical use of parenteral enzymes is bound to grow and there is no doubt that clinical enzymology has come to stay.

F. G. YOUNG

Scientific and Learned Societies of Great Britain

A Handbook compiled from Official Sources. 59th edition. Pp. 215. (London: George Allen and Unwin, Ltd., 1958.) 35*s*. net.

THIS book, the third of its kind, derives from the "Yearbook of Scientific and Learned Societies", which ceased publication in 1939 after appearing almost continuously for more than fifty years. It is now edited by the British Council.

The greater part of the book consists of a list of nearly a thousand societies, ranging from the Royal Society down to the small local natural history societies, grouped under sixteen headings. Particulars of the objects, membership, meetings, publications, museum and library of each society are given. Some of the entries are of societies not strictly scientific, but inclusion is no doubt preferable to omission in compilations of this sort. The criterion is, in general, whether a society gives educational facilities to its members, or publishes original work.

There is also a list of the principal organizations conducting officially sponsored research, and a select bibliography on the organization of scientific research in Great Britain. In the former, universities, technical colleges and laboratories attached to commercial firms are, of course, not included; but neither are the industrial research organizations. These are officially sponsored since they receive Department of Scientific and Industrial Research grants, and they might usefully be brought into future editions.

BIOSYNTHESIS AND CONSTITUTION OF LIGNIN*

By Prof. KARL FREUDENBERG
University of Heidelberg

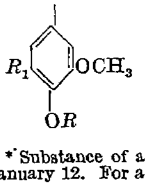
NEARLY forty years ago, by studying the kinetics of the degradation of cellulose, I obtained evidence that there exists a clear order in the large cellulose molecule, one glucose unit being bound to the next in the same way as in cellobiose[3]. This concept of a *uniform* chain, which was later adopted by H. Staudinger and W. N. Haworth, encouraged me to attack lignin, the other major wood constituent.

The problem was to decide whether lignin is a sort of molecular 'compost heap', or whether, like cellulose, it possesses an orderly structure. The second possibility was preferred as a working hypothesis.

However, lignin is a condensed system which cannot be hydrolysed, and the units from which it is built, though of similar types, are not identical. Analytical efforts to elucidate the lignin structure made but slow progress. It contains methoxyl[4], hydroxyl, and ether[5] groups, and can give 30 per cent of the theoretical yield of vanillin[6]. Formaldehyde[7] and *iso*-hemipinic acid (3-carboxy-4,5-dimethoxybenzoic acid)[8] are other products of degradation, and Hibbert[9] isolated a small amount of ketones by alcoholysis. In 1935, Holmberg[10] discovered that phenylcarbinol groups and their ethers are involved in the sulphite pulping process, and the Swedish school elucidated the specific nature of the phenylcarbinols responsible for this important reaction. Among these ethers are phenyl-coumarans, which had been proposed as constituents of lignin[11]. Despite these discoveries, it still remains impossible to construct a constitutional scheme for lignin from purely analytical information.

In 1875, Tiemann in Berlin cleared up the constitution of the glucoside coniferin (I) which is present in the cambium sap of conifers during the period of vegetation. In deciduous trees coniferin is found together with syringin. The present discussion is confined to coniferous wood.

Tiemann suggested that lignin and coniferin are related genetically[12], and this idea was used by Klason[13] throughout his work on lignin chemistry. H. Erdtman[14] showed that the product obtained many years ago by two French workers[15], who oxidized *iso*eugenol by means of mushroom oxidases, was in fact a phenylcoumaran similar in kind to that claimed to occur in lignin. This oxidation reaction provided a model for the formation of lignin, and in 1933 Erdtman[14] pointed out that lignin might be a dehydrogenation product of guaiacyl-propane derivatives with an oxidized side-chain.



(I) R and R_1 = H: coniferyl alcohol

(II) $R = C_6H_{11}O_5$; R_1 = H: coniferin

(III) R = H, $R_1 = OCH_3$: sinapinic alcohol

(IV) $R = C_6H_{11}O_5$; $R_1 = OCH_3$: syringin

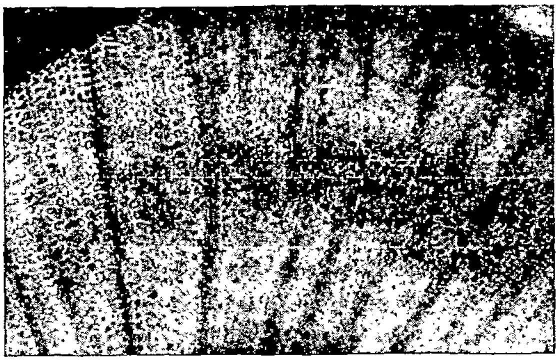


Fig. 1. Cross-section through a spruce sapling after administration of D-coniferin-β-^{14}CH

During the past eight years we have been studying the biosynthesis of lignin by the method of introducing various radioactive substances into spruce saplings. The needles of a small side twig are trimmed down, and the twig is allowed to suck up a solution containing the tracer[16]. It is found, when using radioactive D-coniferin, that the radioactivity is fixed within a few days in the region around the point of attachment of the branch, and radioactive lignin is obtained (Fig. 1). Afterwards, normal cells grow over the radioactive ones. Using L-coniferin, prepared from L-glucose and radioactive coniferyl alcohol, no radioactive lignin is obtained[16]. When radioactive phenylalanine is introduced, it is transformed into radioactive coniferin[17], which can be isolated from the plant after one or two days. After a further few days, we find once again that the radioactivity is fixed in that zone of cells which is in the process of lignification at the time of the experiment. It is astonishing how quickly the transformation of the phenylalanine into coniferyl alcohol, and the conversion of the latter to its glucoside, take place. Thus, coniferyl alcohol is derived from an acid of the C_6C_3 group, precursors of which are shikimic and prephenic acids.

We have, therefore, at our disposal ordinary natural lignin isolated from wood, lignin produced in the tree in the presence of radioactive coniferin, and lignin similarly formed in the presence of phenylalanine. Both coniferin and phenylalanine can be labelled at different carbon atoms.

But there is also a way of preparing lignin *in vitro*. If air is bubbled through a very dilute aqueous solution (less than 0·5 per cent) of coniferyl alcohol in the presence of mushroom laccase, at 20° C. and *p*H 5·5–6·5, a light grey-brown precipitate is formed. Depending on the enzyme concentration, the time required may be minutes or hours. The precipitate accounts for 80–90 per cent of the coniferyl alcohol used. From it some substances of low molecular weight can be extracted by butanol at ordinary temperatures, and the residue is biosynthetic lignin produced by enzymatic dehydrogenation of coniferyl alcohol. Cambium laccase can be used instead of mushroom laccase[19], and the biosynthesis can also be effected by means of horse-radish peroxidase and very dilute hydrogen peroxide solution[19]. Radioactive coniferyl alcohol labelled at different carbon atoms can also be used for these *in vitro* experiments.

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* Substance of a lecture given in the University of Cambridge on January 12. For a recent survey of work on lignin, see refs. 1 and 2.

Our array of lignin preparations suitable for examination is therefore increased by these biosynthetic products. Extensive comparison, both physical and chemical, of the best biosynthetic and natural lignin preparations leads to the conclusion that they are identical in their properties[2,17,20,21]. Analogous degradation products from both were either radioactive or not, depending on the site of the labelled atoms in the monomeric tracer. The molecular weight in both cases was of the order of 10,000. Details may be seen in publications of the Heidelberg school.

The middle part of Fig. 2 represents a cross-section through the cambium of spruce wood; the cambium cells can be recognized by the nuclei which have been included. On the inner side of the cambium on the right, the delicate, newly formed cells are converted gradually into mature wood, while on the left they form bark. When the cell walls have become quite thick, wood formation is ended. The lower part of Fig. 2 shows a section which has been stained with phloroglucinol and hydrochloric acid. The lignin is [redacted] deep red, and is indicated by dark portions on the drawing. During the vegetative period the tissues of the cambium and adjacent cells contain large amounts of the glucoside coniferin. Laccase and, to a smaller extent, peroxidase, are also present in the cell sap[19]. But these enzymes cannot attack coniferin; they can only build up lignin from coniferyl alcohol. This led to the conclusion that a β-glucosidase must also be present in the tissue, but we were unable to extract it. We therefore used a dilute solution of the synthetic glucoside, indican, which can be split by glucosidase into glucose and indoxyl. Indoxyl on exposure to the air is oxidized to indigo. (M. W. Beijerinck[23] used a somewhat similar method with the sap of *Isatis tinctoria* to indicate the location of emulsin in almond sections.) In our case the blue colour of indigo develops rapidly between the fresh cells and the mature wood (upper part of Fig. 2)[22]. Here are the very cells in which lignification is taking place. The prediction of the presence of a β-glucosidase and its direct observation are a strong argument in favour of our theory of the biogenetic pathway of formation of wood. Coniferin is produced from C_6C_3 acids *en route* from the point of introduction to that of lignification. It diffuses into the newly formed cells, where it is hydrolysed to glucose and coniferyl alcohol, and the latter, coming into contact with laccase and peroxidase, is transformed into lignin. The cell dies as soon as the hollow spaces of the cell wall are filled up with lignin.

To recapitulate: coniferin, which originates from a C_6C_3 acid, is an intermediary substance which is converted by the action of a β-glucosidase into coniferyl alcohol, and this hydroxy-cinnamic alcohol is then transformed by laccase and peroxidase into lignin. Natural lignin and lignin formed *in vitro* are identical. It is thus proved conclusively that spruce lignin is a C_6C_3 substance of the guaiacyl type, but the details of its constitution remain just as obscure as ever.

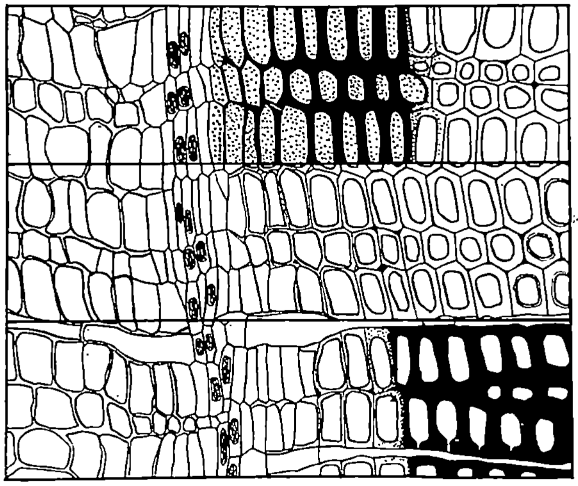
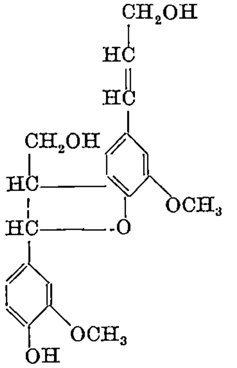


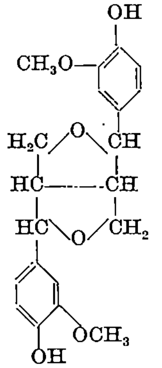
Fig. 2. Cross-section (schematic) through spruce cambium. Middle part unaltered, bottom part treated with phloroglucinol hydrochloride, top part treated with indican

However, there is one more way of approaching this question. As is mentioned above, the crude biosynthetic lignin contains substances of relatively low molecular weight. If lignin formation is interrupted at a certain stage, namely, when all the coniferyl alcohol has been used up and only very little lignin has been formed, a large amount of these intermediates of low molecular weight is obtained. The intermediates of the *in vitro* preparation form the vital key to the *in vivo* processes of lignin synthesis. So far, the following intermediates have been isolated[24–27]:

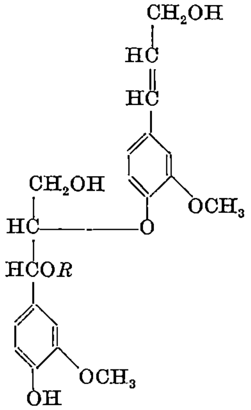
(*A*) dehydro-diconiferyl alcohol (V); approximate amount 20 per cent of the original amount of coniferyl alcohol; (*B*) DL-pinoresinol (VI); about 20 per cent; (*C*) guaiacylglycerol-β-coniferyl ether (VII); about



(V) Dehydro-diconiferyl alcohol (substance *A*)

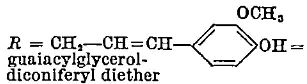


(VI) Pinoresinol (substance *B*)



(VII) *R* = H : guaiacylglycerol-β-coniferyl ether (substance *C*)

(VIII)



$R = CH_2—CH=CH—$ OH =
guaiacylglycerol-diconiferyl diether (substance *H*)
(XIII) $R = CH_3$
(XIV) $R = C_{12}H_{21}O_{10}$

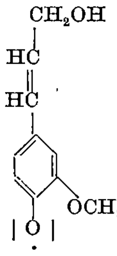
30 per cent or more ; (*D*) coniferyl aldehyde (1 per cent) ; (*E*) the aldehyde of V (4 per cent) ; (*F*) the aldehyde of VII (3 per cent) ; (*G*) dehydro-dipinoresinol (4 per cent) ; (*H*) guaiacylglycerol-diconiferyl diether (VIII) ; 15 per cent. A further product (*J*) is guaiacyl-glycerol-β-coniferyl-γ-dehydro-diconiferyl-diether, corresponding to (VIII). The yield of each substance has its individual maximum at a different stage of formation of lignin. Addition of the percentages quoted above would be misleading.

Other intermediates are still under investigation. The substances *A*, *B* and *C* are the major constituents of the mixture ; *E*, *F*, *G* and other products are derived from these three ; *G* is a diphenyl derivative, built up of two molecules of (VI), minus two hydrogen atoms. In addition to these substances, the presence of many others, the total quantity of which is small, can be demonstrated by paper chromatography. By the continued action of the enzymes, these substances are dehydrogenated further and condense with each other or with coniferyl alcohol to form the lignin polymolecule[30]. A subsidiary amount of linking may be caused by a simple addition without loss of hydrogen. This is the case with substances *H*, formula (VIII), and *J*. There is evidence that such a condensation occurs through the addition of the primary carbinol group of coniferyl alcohol to a quinone methide group (formula XII, see below).

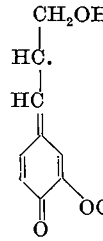
The above formulæ contain all the elements of structure which are necessary to explain the chemical behaviour of lignin : (VII) contains a phenyl carbinol group, (VI) and (VIII) contain aliphatic benzyl alkyl ethers, and (V) is a benzyl aryl ether. These groups are involved in the sulphite and sulphate pulping processes. Cinnamic aldehyde groups, which are responsible for the colour reactions of lignin, are also present. *Iso*hemipinic acid is obtained from (V) and is radioactive when the β-carbon atom of the coniferyl alcohol side-chain is labelled with carbon-14[17]. It is noteworthy that all these intermediates as well as lignin itself are optically inactive.

It is not difficult to explain the origin of all of these substances. Enzymatic attack on coniferyl alcohol causes the removal of a phenolic hydrogen atom, leaving a radical which can be written in various mesomeric forms, including (IX), (X) and (XI). Structures (X) and (XI) can combine to form a quinone methide which, by rearrangement, yields (V), while two units of the limiting structure (X) can combine and become rearranged to pinoresinol (VI). Similarly, (VII) could arise from the combination of (X) and (IX), followed by the addition of water to the resulting quinone methide (XII). With coniferyl alcohol, (XII) forms the labile substance (VIII)[27], and similarly with methanol or cane sugar, (XIII) and (XIV) result ; these have been isolated.

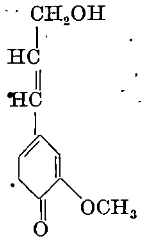
So far, it has not been possible to furnish direct evidence for the formation of the radicals ; their dilution is too great and life-time probably much too short. The quinone methides have been observed recently by direct ultra-violet measurements[28], and their half-life is estimated at about 60 min. under the conditions of measurement. Well-founded chemical evidence for the intermediate formation of (XII) has also been obtained. If the enzymatic dehydrogenation of coniferyl alcohol is carried out in water containing 30 per cent methanol, a new substance appears among the regular ones[28]. It is the γ-methyl ether (XIII) of (VII), and is formed by addition of methanol to the quinone methide (XII), thus providing direct proof of the transitory existence of (XII). *J* is an addition product of (XII) and *A*. Even cane sugar can be added to (XII) in the same way, the product being (XIV)[28]. This demonstrates the manner in which lignin is combined with the carbohydrates of the cell wall.



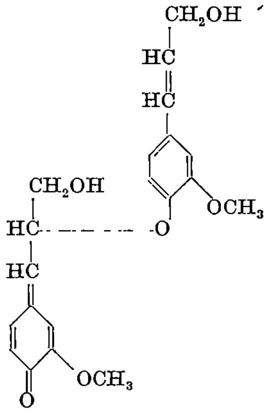
(IX)



(X)



(XI)



(XII)

The theory of lignin constitution developed above explains why the C_6C_3 units in conifer lignin, although originating from a single substance, namely, coniferyl alcohol, occur in such a vast number of different forms. Another remarkable fact is that lignin and also the intermediates, despite their many asymmetrical atoms, are all optically inactive. This is also explained by the intermediate formation and mesomerism of the radicals, which are optically inactive. The action of the enzymes is restricted to dehydrogenation of phenolic groups. All subsequent reactions, such as the formation of quinone methides by the interaction of the radicals, the addition reactions of the quinone methides and possibly polymerization reactions, proceed automatically without further regulation by enzymes. Even a solution of copper sulphate in water transforms—albeit slowly—coniferyl alcohol in the presence of oxygen into the same intermediates, and finally into lignin.

It has been mentioned above that the enzymatic dehydrogenation of coniferyl alcohol does not yield biosynthetic lignin quantitatively. The reason is that, even during the course of its formation *in vitro*, the lignin is partially degraded by further dehydrogenation. When a fine suspension of either natural or artificial lignin in water is subjected to the dehydrogenating activity of the enzymes[19] laccase or peroxidase, it undergoes the same degradation. This process is closely related to humification and destruction of phenols in the soil. Lignin can therefore be built up and degraded by the same enzymes. In the organized system in the plant, only formation occurs, because the action of the enzymes ceases when the tissue has been filled up with lignin. But when the dehydrogenases approach from external sources, as in the case of attack by wood-rotting fungi, the degradation process sets in. Hence it is understandable why mushrooms and wood-rotting fungi contain laccase and peroxidase — preferentially in the mycelium and stipe—although they do not produce lignin. They require the laccase for the degradation of lignin or other phenolic substrates of the soil or wood.

Lignin of deciduous wood is built up of a dehydrogenated mixture of coniferyl and sinapinic alcohols (I and III). Sinapinic alcohol, which occurs in trees as its glucoside syringin (IV), has never been found as the exclusive building unit for a natural lignin. The explanation is given by the following experiment. When laccase or peroxidase acts on sinapinic alcohol, 80–90 per cent syringa-resinol (5 : 5′-dimethoxy derivative of pinoresinol, VI) is formed[19,29]. The residual 10–20 per cent consists of the same degradation products as are obtained when pure syringa-resinol is exposed to dehydrogenase[19]. Obviously the intermediates containing phenyl ether bonds corresponding to (V) and (VI) cannot be formed owing to steric hindrance. Following enzymatic degradation of syringa-resinol, 3 : 5-dimethoxy-*p*-quinone has been [redacted][19].

The question is therefore answered as to whether lignin has an intelligible structural principle, and it is also explained why its architecture is more intricate than that of any other polymolecule[30]. So far, the principles involved in the formation of lignin have not been applied to the technical synthesis of other materials.

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INFLUENCE OF THE ANTERIOR PITUITARY ON THE AGEING PROCESS IN THE OVARY

By DR. E. C. JONES and PROF. P. L. KROHN*

Department of Anatomy, University of Birmingham

TWO alternative ways of defining and measuring the rate of ageing are open to us. The first is an actuarial analysis of the increasing vulnerability of an ageing population. The second is based on the individual, and attempts a causal analysis of the ageing process at a chosen level of biological organization. For this purpose a particularly suitable method is to form heterochronic chimeras, in which tissues of one age are transplanted into the environment of another age. It is obviously desirable to choose a system for study which shows clear-cut signs of deterioration with age, but the visible changes that can be expressed quantitatively vary widely from one system to another. The central nervous system is one which could possibly be studied, and Burns[1], making use of Brody's[2] figures, has calculated that 100,000 neurones are irretrievably lost from the human cerebral cortex every day. The glomeruli in the kidney probably constitute another field of study. But neither appears to provide as advantageous a situation as does the female reproductive system, where the changes in overall reproductive capacity are very easily measured and can be correlated with a gradual loss of oocytes from the ovaries.

It has been universally accepted that the ovaries finally lose all the oocytes which they once contained. But since the middle of the nineteenth century there has been vigorous controversy about whether neo-formation during adult life can add to the original complement or whether the female has to make the best she can of a limited number of oocytes with which she is endowed in early life. The problem has been exhaustively reviewed from time to time as opinion has oscillated in favour of one theory or the other. The most notable recent reviews[3,4] have been based on a series of quantitative observations and planned experiments which decisively tip the balance in favour of the endowment theory. These data clearly show that the decline in the total number of oocytes begins early in life and continues regularly with increasing age. They also show that no experimental situation has been contrived in which any part of the ovary can be convincingly demonstrated to give rise to fresh oocytes.

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* Nuffield Senior Gerontological Research Fellow.

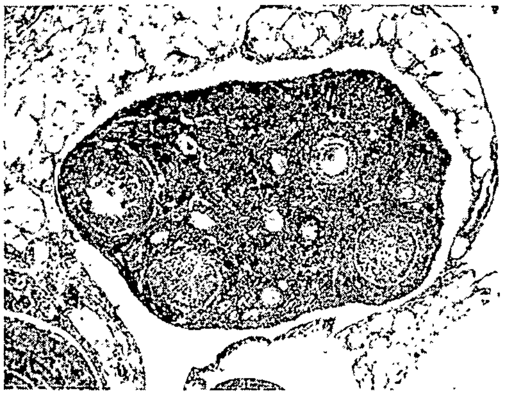

Fig. 1. Ovary from 346-day-old *CBA* strain mouse hypophysectomized 264 days earlier. (× 60)

Like the neurones, therefore, the female germ cells appear to be unable to reproduce themselves by mitotic division and are irreplaceable. It is because an understanding of this limiting factor would have such relevance to the study of the pattern of fertility that an analysis of the processes underlying the disappearance of oocytes has been undertaken.

Removal of oocytes at ovulation, and the atresia of other Graafian follicles which, for reasons that are not yet clear, fail to ovulate, can readily account for some of the loss. The decline in numbers, however, is too great and begins too early in life (immediately after birth in mice and rats), when there are no large follicles, for this factor to do more than provide a partial explanation. It has long been apparent that the major part of the loss must be due to some different process that affects the small follicles.

In addition to controlling the loss of oocytes at ovulation, it is possible that the pituitary may have a further influence on the ageing process in the ovary. The limited purpose of the present experiments was, therefore, first—to compare the rates of loss of oocytes in normal and hypophysectomized mice ; and second—having established that hypophysectomized animals lose their oocytes more slowly, to show by transplantation methods that the oocytes in ovaries, whose rate of ageing has been retarded by hypophysectomy, remain fully viable, even when their chronological age is greater than the age at which reproduction has ordinarily ceased. The labour involved in counting, and the limitations imposed by immunological considerations virtually restrict one's choice of animal in experiments of this kind to the mouse. All the experiments reported here have been carried out on mice of the *CBA* strain, whose exceptionally rapid normal loss of oocytes makes them particularly convenient to use. Further studies (to be reported elsewhere) have shown that the influence of hypophysectomy on the numbers of oocytes also extends to other strains (*A* and *R*III and hybrid crosses) in which we have not yet, however, carried out transplantation experiments.

Methods and Results

The mice were hypophysectomized at an average age of 39 days by Thomas's[5] method. Only those the sellæ turcicæ of which were shown by serial sections at the end of the experiment to be free of pituitary remnants have been included in the results. The technique adopted for counting the oocytes was the same as that used by Mandl and Zuckerman[6] in rats.

The results of the counts in 52 normal *CBA* mice, ranging in age from 1 to 437 days, can be expressed by the equation :

$$\log y \text{ (total number of oocytes)} = 4\cdot049 - 0\cdot00711\, x \text{ (days)}$$

and for 16 hypophysectomized *CBA* mice aged from 44 to 346 days at autopsy :

$$\log y = 3\cdot735 - 0\cdot00247\, x$$

The two regression coefficients are significantly different from each other ($P < 0\cdot001$). They imply that normal *CBA* ovaries lose about 30 per cent of their population of oocytes every 20 days and hypophysectomized animals only about 10 per cent. For example, the ovaries of a 320-day old normal *CBA* mouse would be expected to contain about 70 oocytes whereas the ovaries of a hypophysectomiz[redacted] of the same age would contain about 880 oocytes—more than 12 times as many. The histological differences between the two types of ovary are exemplified in Figs. 1 and 2. The ovary of the hypophysectomized mouse (Fig. 1) is much smaller and contains neither large follicles nor corpora lutea. But there are far more small oocytes in it, and the usual signs associated with ageing in the ovary (for example, ceroid, pigment and anovular follicles) are much reduced.

There are no precise histological criteria which permit one to distinguish categorically between normal and atretic small follicles. Nevertheless, an attempt was made to separate the two categories when the original counts were being made. The ratio of normal to atretic small follicles was found to be 74 : 26 in hypophysectomized *CBA* mice and 49 : 51

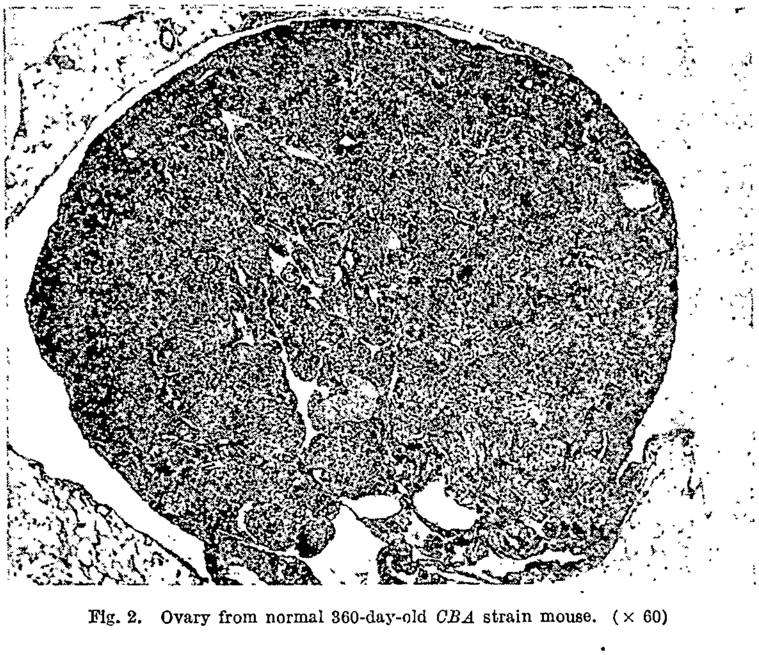

Fig. 2. Ovary from normal 360-day-old *CBA* strain mouse. (× 60)

in normal mice. Afterwards, five observers who were not told that the sample contained ovaries from hypophysectomized animals were asked to estimate the ratio of normal to atretic follicles in a smaller sample. They evidently varied in the subjective criteria which were used to assess the normality of an oocyte, since the proportion thought to be normal differed, but all agreed that the proportion was greater in those ovaries which had come from hypophysectomized animals.

The reproductive capacity of the ovaries of the hypophysectomized mice was tested by transplanting them orthotopically into young and old mice of the same strain, using a surgical technique which will be described elsewhere.

The first host mouse was a 456-day old *CBA* female which had given birth to 8 litters, the last 2 months earlier. Her ovaries, which were removed immediately before the unilateral orthotopic transplantation, contained only anovular follicles and remnants of corpora lutea. The hypophysectomized donor of the transplanted ovary was 311 days old and had been hypophysectomized for 273 days. The number of oocytes in the transplanted ovary was estimated from the regression equation at 460.

The host had previously shown irregular periods [redacted] cornification ; her cycles remained infrequent and irregular after the grafting operation. She was paired with a male of proved fertility but never showed any signs of having mated.

The ovarian pad of fat, containing the graft and Fallopian tube, was removed 72 days later for histological examination. Serial sections showed that the operation had been technically successful, in that there were no obvious barriers to the free passage of ova from the graft to the Fallopian tube and uterus. The graft had enlarged and, among the total of 270 follicles which remained, contained 7 follicles with antra. There were, however, no corpora lutea nor signs of luteinization and the nuclei of stromal cells retained the cartwheel appearance, typical of a deficiency of luteinizing hormone, which is found with increasing frequency as animals get older[7].

Three young spayed virgin *CBA* females were given single orthotopic ovarian transplants. The first was 62 days old and received the second ovary from the hypophysectomized mouse which had provided the graft for the old mouse referred to above. Evidence that the graft was producing œstrogen soon appeared, the vaginal smear being fully cornified within a week. An interval of pseudo-pregnancy followed mating, and was succeeded by a pregnancy which resulted in the birth of three normal young. A second litter of two died, but a third litter of six was entirely healthy. The grafted ovary was 437 days old when the third litter was born, an age which is well past the average (352 days) at which reproduction ordinarily ceases in the *CBA* strain of mice.

The other two young females (92 days old) received single transplants (estimated to contain 290 oocytes each) from a 392-day old mouse hypophysectomized 354 days earlier. Vaginal cornification returned 4 and 5 days after the operation. One mouse has given birth to two litters, each containing two young, the second litter being born when the grafted ovary was 498 days old. The other mouse has mated repeatedly and has shown a succession of pseudo-pregnancies without becoming pregnant. It is assumed that adhesions have developed between the surface of the graft and the ovarian capsule which prevent the eggs from reaching the tube. This unfortunate complication of the operation is fairly common.

Discussion

The results show that after hypophysectomy oocytes are lost much more slowly from the ovary and that the proportion of small follicles showing the histological signs of atresia decreases. The ageing process, as it affects the ovary of the mouse, is therefore retarded when the pituitary is removed.

Earlier studies of the effect of hypophysectomy on the number of oocytes in the ovary purported to show that the number actually increased after hypophysectomy in rats[8,9]. The experiments were not, however, intended to show any relationship between pituitary secretions and the destruction of oocytes by atresia, but to prove that the pituitary ordinarily prevents the ovary from engaging in the neoformation of oocytes at the rate it would choose if freed from restraint. However, Ingram's[10] much more satisfactorily controlled experiments failed to confirm the observations on which this conclusion was based. Instead they clearly demonstrated that the number never exceeded the normal pre-operative control figures, and indeed, continued to decline after hypophysectomy. Although Ingram's hypophysectomized rats did lose their oocytes more slowly than the normal animals, he was unable to show that the difference between the two regression coefficients relating age and numbers of oocytes was statistically significant.

Our results can best be explained by assuming that hypophysectomy removes an unidentified atresia-promoting factor in addition to stopping the loss from ovulation. An alternative but more cumbersome explanation would be that some extra-pituitary factor is no longer able to act, the pituitary hormones normally playing the sort of permissive part which is sometimes attributed to adrenal cortical hormones in other endocrinological situations. It seems unlikely that the factor is any one of the gonadotrophins since the rapid loss of small follicles by atresia in the normal animal precedes any evidence that gonadotrophins are being released by the pituitary. It is tempting to choose somatotrophin from among the recognized hormones of the anterior pituitary, on the basis of its known influence on cellular growth and differentiation. At present there is, however, no experimental justification for such a choice.

But the population of oocytes does not remain intact even after the removal of the atresia-promoting factor by hypophysectomy. On the contrary, the negative slope of the regression line differs significantly from zero, and oocytes continue to be lost, even if more slowly than normal. It must therefore be assumed that yet another unknown process, which is independent of the pituitary, promotes the loss of oocytes. Ageing of the ovary, as measured by the overall loss of oocytes, therefore depends on the combined effects of at least three separate factors—one concerned with the maturation of follicles for ovulation, a second unidentified pituitary principle and a more general influence whose effect persists in the absence of the pituitary. As mentioned earlier, the cell populations of several of the other organs in the body are subjected to a process of attrition with the passage of time. Analysis revealed that this process, as it affects the ovary, has a complex structure, but no one knows how far the behaviour of the ovary is unique, or how far it represents a pattern which also applies to these other organs. Only further experiments can decide whether, for example, the decline with age in the number of cortical neurones is retarded by hypophysectomy and whether some loss of cells persists even in the absence of the pituitary.

The transplantation experiments reveal, in addition, that the oocytes and follicles which remain after long-term hypophysectomy are entirely viable and do not necessarily deteriorate simply with the passage of time. They respond normally to the appropriate gonadotrophic stimuli; the follicles ovulate and if the ova are fertilized they are capable of developing into normal young. Equally, the corpora lutea which develop from old granulosa cells are able to maintain a normal pregnancy.

The behaviour of grafts of ovaries from a hypophysectomized mouse depended entirely on the nature of the environment in which they were placed. In an old host the ovary failed to do more than show that its small follicles could grow to Graafian size, whereas complete reproductive capacity was demonstrated in the young host. These observations reinforce earlier suggestions that, although the pituitary continues to produce gonadotrophins, it no longer does so in the proportions which are necessary for reproduction. In particular, it suggests the possibility that the production or the release of ovulating and luteinizing hormones is impaired.

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OBITUARIES

Mr. Frank Twyman, F.R.S.

The scientific world is the poorer for the passing of Mr. Frank Twyman on March 6. He was born in Canterbury in 1876, and attended Simon Langton's School in that city. He went to the Finsbury Technical College and later as Siemens Scholar to the Central Technical College, London. He then obtained a post as cable tester in the Fowler Wiring Cables Co., but he found the work irksome, especially night shifts, and went to Otto Hilger, as he characteristically put it, to "have a rest". (Later he described the work as "a most complicated way of earning a living".) Otto Hilger had succeeded his brother Adam in charge of the firm of Adam Hilger; he died in 1902 and the management passed to Twyman, although only twenty-six years old at the time. Two years later the firm was incorporated with Twyman as managing director, a post which he held until 1946. In 1948 the firm amalgamated with E. R. Watts and Son, and he served as a director until 1952, after which he became technical adviser.

Twyman was a man of tireless energy; until 1910 he designed all the new instruments completely, making all detailed drawings and testing and adjusting the instruments himself. He made many innovations in the production and testing of high-quality components, and was always vigilant in seeking new methods. He believed in sharing his knowledge with others, and for this reason published his book, "Prism and Lens Making". His developments in interferometers for testing optics alone would entitle him to a high place in innovation in industry. Twyman had a deep knowledge of glass-making and an original outlook which benefited makers of high-quality optical glass. He helped to start the Optical Materials Committee, which was of great value during the First World War.

Twyman's outstanding achievement was in the field of spectrochemical analysis. Although the possibility of the use of spectroscopy for chemical analysis, particularly of metals, had been known since the middle of the past century, it had not found favour. He became convinced of its importance, and in 1904 produced the constant-deviation spectrometer with the wave-lengths of the lines displayed on a helical drum. This was a success, bu[redacted]h analysts. The range was restricted to the visible region, whereas the lines of most interest for metal analysis lie in the ultra-violet. Therefore, he designed the fixed medium quartz spectrograph, which shows a wide range of wave-lengths on a photographic plate, and also a large quartz spectrograph of greater dispersion. These appeared in 1910, but with one exception (the American Brass Co.) he failed to persuade analysts of their usefulness, although ready sales were made for academic purposes. Two events broke the deadlock: the American Brass Co. published the results of nine years successful routine-control of brass production, and two firms, one in Germany and one in the United States, made equivalent instruments and inspired the publication of investigations made by means of them.

He was also busy with work in other regions of the spectrum. He made vacuum ultra-violet spectrographs, the first going to Bohr's laboratory in Copenhagen. Against the advice of Paschen, who affirmed that the infra-red region would never be of industrial interest, he made an infra-red instrument, the first of several. X-ray spectrometers were made for Laby and others, and instruments for the investigation of crystal structures by X-rays.

Twyman was elected a Fellow of the Royal Society in 1924. The John Price Weatherill Medal of the Franklin Institute of Washington was presented to him in 1927, the Duddell Medal of the Physical Society in 1927 and the Gold Medal of the Society of Applied Spectroscopists of the U.S.A. in 1956.

He was interested in general matters also, bringing an original mind to bear upon economics and education. He published a small book entitled "Some New Proposals for the Amelioration of the Balance of Payments Position", and another called "Apprenticeship for a Skilled Trade". He was interested in music, gardening, literature and the theatre, and had a wide knowledge of old music-hall songs. For many years his lunch consisted of a glass of milk, which he drank to the accompaniment of his violin—he used to explain that he was "trying to become a third-class amateur". Those who worked with him knew that his apparent ingenuousness hid a clear appraisal of the situation; when a junior brought him a problem, he would say, "and what do *you* recommend?" It is no wonder that he was much loved and respected by his staff. A. C. MENZIES

Prof. Thomas Thomson

WITH the recent death of Prof. T. Thomson we saw the passing of a person who, with singular devotion, had spent his whole life in the service of one educational institution.

When Thomson, a Londoner, entered the University College of North Wales, Bangor, in the first decade of this century, he was somewhat older than the average run of students at the time, and after reading for honours in chemistry, and taking a first, he continued to read forestry under Prof. Fraser Story, then head of that Department.

During the First World War, Story was called to London, and Thomson worked in Wales on problems of woodland felling and timber supplies. This gave him an admirable introduction to the Welsh countryside and to the mind of the countryman, a most valuable asset early in a professional career.

In 1919, the Forestry Commission was set up. Story stayed on in London as its education officer and Thomson returned to Bangor to take charge of the Forestry Department, first as an independent lecturer and latterly, before his retirement, eleven years or so ago, as professor. This was a period of expansion and adaptation in the subject, to meet the new and expanding economy of the new State forest policy in Britain, together with the continuance of training of forest officers for work in the Dominions and overseas.

It was also the period of transfer of activities from the Old Buildings in the Penrhyn Arms Hotel to the Memorial Buildings in Deiniol Road in the mid-twenties. It also witnessed the ever-expanding provision of field courses of training, extramural to the Department at Bangor. Before the War there had been established at Penisa'r Glyn near Chirk in the Ceiriog Valley, Denbighshire, an experimental forestry unit, in the layout of which Thomson was the prime mover. Now, after the War, there followed comprehensive and extensive practical forestry courses in the field in the French State forests, with their long established and tested traditions. This was eventually extended to embrace collateral courses in the newer State forests of Britain, as these developed and matured.

As an academic discipline the subject suffered severely at this time from the serious lack of authoritative standard text-books in English. This Prof. Thomson set himself to remedy, and in due course appeared his English translation of the classic text of "The Foundations of Silviculture" from the German of Busgen and Munch. This was followed by Thomson's own "Outline of Forestry", less ambitious in scope, but withal a very worthy students' manual.

During the Second World War, and the second severe onset on the native timber resources of Britain in one short generation, Thomson gave admirable service, outside his Department, in operating the State scheme of grants for new planting and replanting of timber trees. His thorough and extensive knowledge of conditions in the field in Wales, based on his initial experience during the First World War and extended since, and his natural endowments in the field of human relationship made him a first-rate agent in working this policy—indeed a very successful ambassador among estate and woodland owners.

He had retired from the chair before the Department made its second move to the present site at the corner of Deiniol Road and Glanrafon Hill, but it gladdened his heart to see, so firmly established and so full of promise to the future, a pulsating and virile school that he had done so much to bring into being and to support in its infancy.

Prof. Thomson served his College well in the field of internal administration—a field of service he rather delighted in—as curator of the College grounds, in Board of Faculty, in Senate and as Dean. He was never forward in the rough and tumble of argument and advocacy in the early stages of discussion of any issue, but invariably he came in towards the end with words of wisdom and sagacity. He was a very sound dialectician, a loyal colleague and a sturdy pillar of the Old Students' Association of the College.

Prof. Thomson was twice married, first to Miss Gwen Phillips, eldest daughter of the late Reginald W. Phillips, first professor of botany in the College, and secondly to Miss Connie Izard, a member of the College Music Trio, who survives him.

R. ALUN ROBERTS

Mr. Cyril Barnard

MR. CYRIL CUTHBERT BARNARD, librarian of the London School of Hygiene and Tropical Medicine, and author of the Barnard system of classification for medical libraries, was killed in a road accident on March 6. Son of Harry Barnard, an artist specializing in the design of Wedgwood ware, he was born at St. Margaret's, Middlesex, on July 23, 1894, and was educated at the Stationers' Company School and at the London School of Economics. In 1914, he became a library assistant at the Royal Society of Medicine and in 1918 assistant librarian at the Wellcome Historical Medical Library. During 1921–28 he served as librarian of the Tropical Diseases Library, and in 1929 took charge of the library of the London School of Hygiene and Tropical Medicine in its new building in Keppel Street.

Mr. Barnard graduated B.A. (London) with honours in 1922, and two years later obtained the diploma of the School of Librarianship. In 1931, he was awarded the honours diploma of the Library Association for a thesis entitled "A Classification for Medical Libraries", which was published in 1936. A second enlarged edition, "A Classification for Medical and Veterinary Libraries", came out in 1955. Mr. Barnard was elected a Fellow of the Library Association in 1925, served on the Council of the Association and as secretary of its University and Research Section, and in 1947 became chairman of the newly created Medical Section. In 1953, he was joint honorary secretary of the First International Congress on Medical Librarianship held in London. In 1952, he was invited by the World Health Organization to reclassify its library at Geneva according to his system. At his own library, which his expert knowledge and his devotion made one of the finest of its kind in the world, he introduced special courses of instruction in the use of the library for students.

A member of the Society of Friends, linguist, historian, and a friendly, cheerful, approachable, and quietly firm personality, Mr. Barnard will be greatly missed in medical library circles. W. R. BETT

NEWS and VIEWS

Anti-Locust Research Centre:

Dr. B. P. Uvarov, C.M.G., F.R.S.

Dr. Boris Petrovitch Uvarov, who recently retired from the directorship of the Anti-Locust Research Centre, London, was born in Uralsk in 1888. At the end of the First World War he was a lecturer in zoology and entomology at the Georgian State University, Tiflis. He had already had a distinguished career in Russian entomology following his graduation at the University of St. Petersburg. It was while working as director of the Stavropol Bureau of Entomology on the control of locusts in 1912 that he recognized the conspecificity of two 'species' of locusts as the solitary and swarming phases of *Locusta migratoria*, a discovery which was to revolutionize work in this field.

Uvarov was also keenly interested in Acridid taxonomy, so that he was able to accept the invitation extended to him in 1920 by Dr. G. A. K. Marshall, director of the Imperial Bureau of Entomology, to work in London. As assistant entomologist and later as senior entomologist he worked at that Institute on the identification of Orthoptera and Hemiptera at the British Museum (Natural History). During this time he published numerous important papers on the taxonomy and biogeography of the Acrididae which brought him much acclaim and he rapidly became the world authority on this family. But Uvarov was more than a taxonomist, and such works as "Locusts and Grasshoppers" (1928), "Insect Nutrition and Metabolism" (1928) and "Insects and Climate" (1931) placed him in the forefront of entomological workers.

Meanwhile, the control of locusts was becoming more and more important and he began to devote most of his time to studying this problem. Towards the end of the Second World War the danger of famine in the Middle East and in East Africa became acute, owing to the desperate shortage of shipping. When, therefore, the Colonial Office set up the Anti-Locust Research Centre in 1945, Uvarov was appointed director. Under his inspired leadership and as a result of very hard work involving extensive travel, the Centre grew from strength to strength and is now generally recognized as the most important institute of its kind in the world. Its great reputation and international influence may safely be attributed to Dr. B. P. Uvarov. He was appointed C.M.G. in 1943, became a Fellow of the Royal Society in 1950 and is now president of the Royal Entomological Society, London. He holds various foreign decorations, including the Chevalier, Légion d'Honneur and Commandeur de l'Ordre Royal de Lion of Belgium.

Dr. T. H. C. Taylor

T. H. C. Taylor, who has been appointed to succeed Dr. Uvarov as director of the Anti-Locust Research Centre, graduated at Reading University College. In 1925 he went out to Fiji as government entomologist to assist Dr. J. D. Tothill in his investigation of the problem of the coconut moth (*Levuana iridescens*), which had been causing extensive damage to the coconut plantations. He travelled widely in Melanesia and Indonesia in search of parasites, and as a result of this work the moth was brought completely under control. The results were published by Tothill, Taylor and Paine in 1930 in a massive report on this classic example of successful biological control. In 1935 he was transferred to Uganda, where he specialized on cotton pests. In 1944 he joined the staff of the Commonwealth Institute of Entomology, becoming assistant director in succession to Dr. W. J. Hall, who had been promoted to director. In 1953 Dr. Taylor joined the Anti-Locust Research Centre as deputy director. Since then he has made many tours of inspection of locust stations in Arabia and Africa.

National Agricultural Advisory Service

Sir Robert Rae, director of the National Agricultural Advisory Service, who is to retire on July 31, was formerly professor of agriculture in the University of Reading (see *Nature*, 153, 400; 1944). In 1944 he was appointed British agricultural attaché in Washington and agricultural adviser to the U[redacted]dom High Commissioner in Ottawa. In 1945 he became provincial advisory officer in the National Agricultural Advisory Service, and was promoted to under-secretary in 1947. He was appointed director of the National Agricultural Advisory Service in 1948.

Sir Robert Rae is to be succeeded as director by Mr. J. A. McMillan, at present senior education and advisory officer. After being wounded in the First World War, Mr. McMillan graduated at the University of Edinburgh in 1919. He afterwards became lecturer in agriculture in the University of Leeds, and agricultural organizer to the Lincoln (Lindsey) and Cambridgeshire County Councils. He was seconded during the Second World War to the Cambridgeshire War Agricultural Executive Committee. On appointment to the National Agricultural Advisory Service in 1946 he became provincial director, Eastern Province. He was promoted to senior education and advisory officer in 1948.

Mr. W. E. Jones, at present director of the National Agricultural Advisory Service in Wales, who will succeed Mr. McMillan, graduated with honours in agriculture at the University College of Wales, Aberystwyth. In 1946 he was appointed to the National Agricultural Advisory Service as a grassland husbandry advisory officer, and in 1950 became county advisory officer. He was appointed deputy director for Wales in 1954, and in 1957 he became director of the Service in Wales.

Mr. H. E. Evans, at present deputy director of National Agricultural Advisory Service in Wales, who is to succeed Mr. Jones, graduated with honours in agriculture at the University College of North Wales in 1934. He then spent six years with the Agricultural Economics Department at Aberystwyth. He was associated with the War Agricultural Executive Committees in England from 1940 until he joined the National Agricultural Advisory Service when it was formed in October 1946. Since then Mr. Evans has had continuous experience of farming in Wales, having served as county advisory officer in both Radnor and Carmarthen and more recently as deputy director of the National Agricultural Advisory Service for Wales.

Institute of Oceanography, Dalhousie: Prof. Ronald Hayes

The National Research Council of Canada has awarded an annual grant of 90,000 dollars to Dalhousie University, Halifax, Nova Scotia, for the establishment of an Institute of Oceanography. All branches of marine science will come under investigation, and opportunities for work at sea will be provided by the Royal Canadian Navy, the Fisheries Research Board of Canada and other agencies. Prof. F. R. Hayes, who has been appointed director of the Institute, took his doctorate under the late Prof. James Johnstone in the Department of Oceanography, University of Liverpool. As a post-doctoral fellow of the Rockefeller Foundation he worked at the Prussian Marine Station at Heligoland and the University of Kiel. He is at present chairman of the Division of Biological Sciences at Dalhousie University, and a member of the Fisheries Research Board and National Research Council of Canada.

Pressing problems of the Second World War brought a marked impetus to oceanography in Canada. Co-operation then established has continued under a Joint Committee on Oceanography with representatives of the Royal Canadian Navy, the Fisheries Research Board and the National Research Council, as well as Defence Research Board and the Hydrographic Service. Demands for expansion in the various fields brought to notice the lack of adequate provision for the training of recruits and for research unconnected with immediate economic aims. The Committee appealed to the National Research Council, and Dalhousie University proposed a programme of work, for which the present grant makes provision.

Staff appointments at Dalhousie will provide for research and teaching at graduate level in marine branches of biology, chemistry, geology, and physics. The oceanographic programme at Halifax is being expanded considerably. In 1958, the 177-ft. research vessel, *A. T. Cameron*, was brought into service. Built by the Fisheries Research Board, she has five laboratories, will accommodate nine scientists and carries a crew of 25. The Fisheries Research Board Atlantic oceanographic group, previously stationed at St. Andrews, New Brunswick, is moving to Halifax. The Naval Research Establishment has available a corvette, C.N.A.V. *Sackville*, and an algerine, C.N.A.V. *New Liskard*. It is anticipated that a second algerine will be assigned to research work. The Canadian hydrographic service has recently announced plans for a 4,200-ton research ship scheduled for completion in 1961. The vessel will carry a crew of 85 and scientific staff of 15–20. She will have ten laboratories and will carry two helicopters. The double hull will be reinforced for navigation in Arctic waters, and she will be fitted for all types of oceanographic research, including core-sampling of the bottom.

On the Pacific coast of Canada the University of British Columbia has operated an Institute of Oceanography for the past decade. A similar grant from the National Research Council will permit a very considerable expansion of the programme there also.

Appointments to National Research Council of Canada

The following new members of the National Research Council of Canada have recently been appointed: Dr. F. R. Hayes, head of the department of zoology at Dalhousie University, Halifax; Dr. A. D. Misener, head of the department of physics, University of Western Ontario; Dr. J. Unrau, head of the department of plant science at the University of Alberta, Edmonton. The vacancies were created by the retirement of Dr. J. H. L. Johnstone, head of the department of physics and dean of graduate studies, Dalhousie University, and by the deaths of Dr. R. S. Jane, president of Shawinigan Chemicals Limited, and Dr. R. B. Miller, professor of zoology, University of Alberta.

Ciba Fellowships, 1959–60

The Advisory Panel of the Ciba Fellowship Trust has awarded the following Fellowships for the academic year 1959–1960: Dr. M. H. Richmond (University of Cambridge and the Medical Research Council) to study at the University of Copenhagen (microbiology); Mr. V. P. Arya (University of Banaras and of London) to study at the Polytechnic, Zurich (chemistry of natural products); Mr. J. F. Counsell (University of Bristol) to study at the University of Göttingen (physics); Mr. G. L. Duncan (University of Aberdeen) to study at the University of Louvain (polymer chemistry); Mr. K. Jones (University of Sheffield) to study at the University of Heidelberg (organic chemistry); Mr. B. L. Mordike (University of Birmingham and of Cambridge) to study at the Max Planck Institute, Stuttgart (physical metallurgy).

Imperial College of Science and Technology: Fellowships

The governing body of the Imperial College of Science and Technology, London, has made the following elections to Fellowship of the College: Sir Lewis Casson, former student of the City and Guilds College; Sir Graham Cunningham, member of the governing body of the Imperial College; Prof. A. Holmes, professor emeritus of geology in the University of Edinburgh, a former student of the Royal College of Science; Sir Christopher Ingold, professor of chemistry, University College, London, former student and member of staff of the Imperial College; Dr. L. B. Pfeil, director of the Development and Research Department of the Mond Nickel Company, former student of the Royal School of Mines; Mr. R. McKinnon Wood, member of the governing body of the Imperial College.

Television Society Premiums

The Television Society has awarded the following premiums, for outstanding papers read before the London meetings during 1957–58: *The Wireless World* Premium to Mr. B. Overton (Mullard Research Laboratories) for his paper on "Transistors in Television Receivers"; the E.M.I. Premium to Dr. R. Theile (Institut für Rundfunktechnik) for his paper on "Recent Investigations into the Operation of Image Orthicon Camera Tubes"; the *Electronic Engineering* Premium to Dr. J. C. Parr (formerly of Kelvin and Hughes, Ltd.) for his paper on "Some Aspects of Waveguide Technique"; the Pye Premium to Mr. L. J. Griffen (Kolster Brandes, Ltd.) for his paper on "Dressing Television: Cabinet Design"; the Mervyn Premium to Mr. K. H. Smith, (Siemens Edison Swan, Ltd.) for his paper on "Performance of Television Receiver Turret Tuners"; the Mullard Premium to Mr. J. Polonsky (Compagnie Générale de Telegraphie sans Fils) for his paper on "A French Portable Television Camera".

Committee on Chemicals, Oil and Gas from Coal

In the House of Commons on April 16, Mr. J. C. George asked the Paymaster-General what further action the Government proposed to take to investigate possible methods of converting coal into chemicals, gas and oil. Sir Ian Horobin, in a written answer, stated that the Minister of Power has decided, after consultation with Sir Alexander Fleck, chairman of the Scientific Advisory Council, to set up a committee with the following terms of reference: "To review the work that has been done in recent years on the development of processes in which coal is the basic raw material and which will produce marketable products of a chemical or a gaseous or liquid hydrocarbon type; and to make recommendations as to the direction of further research and development work on any such processes which appear to the committee to hold promise of industrial application and as to the type of organization or organizations best suited to carry out such work".

The members of the committee will be: *Chairman*, Mr. A. H. Wilson (managing director in charge of research and development, Courtaulds, Ltd.); *Secretary*, Mr. W. R. G. Bell (Ministry of Power); Mr. M. A. L. Banks (director, B.P. Trading, Ltd.); Mr. Henry Benson (Cooper Brothers and Co.); Mr. H. E. Collins (National Coal Board); Capt. (E) W. Gregson (chairman, Fuel Efficiency Advisory Committee); Dr. R. Holroyd (director, Imperial Chemical Industries, Ltd.); Mr. W. K. Hutchison (chairman, South Eastern Gas Board); Dr. M. A. Matthews (Shell International Chemical Co., Ltd.); Mr. B. E. A. Vigers (Laporte Industries, Ltd.). The committee will be assisted in its work by two assessors: Mr. A. W. Clarke (director, Warren Spring Laboratory of the Department of Scientific and Industrial Research); and Mr. D. A. B. Llewellyn (Ministry of Power).

Manufacture of Polypropylene in Britain

An agreement has been signed whereby Imperial Chemical Industries, Ltd., acquires a licence under the Montecatini and Montecatini/Ziegler U.K. patents covering the production and use of a new polypropylene plastic, originally discovered by Prof. Natta. A new plant to manufacture this plastic ('Propathene') is being constructed at the Wilton Works in North Yorkshire. It is expected to bring the total capacity of Imperial Chemical Industries for polyolefines for 'Alkathene' and 'Propathene' to more than 100,000 tons a year. 'Propathene' is being manufactured at a pilot plant, and arrangements have been made to augment this pilot plant production so that the material will be available commercially from June 1. 'Propathene' is particularly suitable for moulding uses in view of its high rigidity and resistance to temperature. It is also expected to find extensive use in film form and as a general extrusion material.

First Hungarian Atomic Reactor

Hungary's first experimental atomic reactor, which began working on March 25, is a small reactor, of 2 MW. capacity, situated in the Buda Mountains above Budapest. The installation is fully automatic. The Soviet Union supplied plans and a large part of the installation, five Hungarian institutes drew up the final designs and thirty Hungarian establishments took part in the construction of the reactor. It is primarily for research work, and particularly for the training of nuclear technicians. Neutrons obtained from the reactor will be used for experimental examination of the structure of the atomic nucleus, and isotopes will be supplied to industrial, medical and scientific establishments in Hungary. Previously, radioactive isotopes required for therapeutic purposes have been obtained abroad, and short-lived isotopes required for biological experiments could not be obtained at all. The reactor will solve both these problems. Experience gained from the new reactor will be used in the future planning and construction of atomic power stations in Hungary.

The National Engineering Laboratory

The Council for Scientific and Industrial Research has announced that in future the Mechanical Engineering Research Laboratory at East Kilbride, near Glasgow, will be known as the National Engineering Laboratory. This is considered desirable in order to emphasize the national character of the Laboratory, which is part of the Department of Scientific and Industrial Research organization and is financed from public funds: it does not imply any change in the field covered by the Laboratory. A Steering Committee has been set up to look after the programme of the Laboratory, the object of which is to extend knowledge of mechanical engineering science so as to provide industry with the information it requires for the solution of its own ~~particular~~ problems. In order therefore that its work may be focused on practical objectives of real value to industry (which may involve basic or applied research or, in suitable cases, development work), it has been decided that the planning of the Laboratory's activities and the selection of research projects can best be under the control of a small body with a measure of executive authority. The Committee's terms of reference are: (1) to be responsible to the Research Council for the selection of projects and for the allocation of effort to them, within the financial resources allocated to the Laboratory and such other limits as may from time to time be imposed by the Council; (2) to report annually to Council, submitting a research programme for the following year. The Committee, which will be a full committee of the Research Council, is empowered to set up specialist sub-committees to provide technical advice on particular fields of work.

The new Steering Committee will be under the chairmanship of Vice-Admiral Sir Frank Mason, (director of Metal Industries, Ltd., and of H. W. Kearns and Co., Ltd.), who is a member of the Research Council and chairman of the outgoing Mechanical Engineering Research Board. The members of the Committee will be Prof. O. A. Saunders (Imperial College of Science and Technology, London), Norman Elce (director of Metropolitan-Vickers Electrical Co., Ltd.), Dr. D. G. Sopwith (director of the Mechanical Engineering Research Laboratory), Dr. C. M. Cawley (director of Stations and Grants Divisions of the Department of Scientific and Industrial Research). In order to assist the Director as the Laboratory expands and to improve and extend the links between the Laboratory and industry, two deputy directors have been appointed. They are Dr. S. P. Hutton and Mr. F. D. Penny. Dr. Hutton, who is at present head of the Fluid Mechanics Division of the Mechanical Engineering Research Laboratory, will have special responsibilities for fostering closer relationships with industry. Mr. Penny, who is chief development engineer at the Fuel Research Station, will be responsible for the management of the research programme.

Technical Assistance Programmes

At the request of the International Co-operation Administration, the U.S. National Academy of Sciences—National Research Council has undertaken a study of the ways in which science and technology can most effectively be used by the Administration in its assistance programmes for Africa south of the Sahara and north of the Union of South Africa. Leaders in scientific and technological research and African studies have been asked to assist in the evaluation of opportunities for the utilization of research in the fields of public health, medicine, agriculture, natural resources, engineering and education. A final report will be submitted by June 1959. Dr. J. George Harrar, director for agriculture at the Rockefeller Foundation, has been appointed executive director of the study.

Laboratory Equipment in American Schools

Teachers of science in American colleges, universities and non-profit-making organizations have been invited by the National Science Foundation to submit proposals for the construction of better laboratory equipment for use in schools. Under the terms of a new, experimental programme, the Foundation will consider proposals for the design and construction of improved laboratory equipment and for the development of new instructional materials for lecture demonstrations, laboratory and field work for courses at elementary and secondary school, and undergraduate levels in mathematics, astronomy, earth sciences, physical and biological sciences, and engineering. Support will not be provided for the purchase of equipment for renovating school and college laboratories, or for commercial production of equipment or materials.

Nigeria Science Association

As a result of the rapidly increasing volume of scientific work in Nigeria, many scientists have for some time felt the need for a Nigeria Science Association. In October 1957 a meeting was called at the University College, Ibadan, to discuss the matter. After a further meeting in January 1958 it was decided that a Science Association of Nigeria should be formed and should hold its inaugural meeting in December 1958. A steering committee was elected, with Prof. J. Grayson, professor of physiology at University College, Ibadan, as chairman, and Dr. Brian Hopkins, lecturer in agricultural botany at University College, Ibadan, as secretary. The inaugural meeting of the new Association was held at University College, Ibadan, during December 15–19, 1958. At a brief but impressive opening ceremony, which was well attended, the Association was inaugurated by the Hon. Victor Mukete, Federal Minister for Research and Information. The opening ceremony was followed by a conference lasting four days. The first three days were devoted to papers and discussions of general interest and to business meetings, and the last day to specialist sections. Four specialist sections were organized: medical sciences, physical sciences, botany and zoology. At the business meeting, Dr. Eni Njoku, Department of Botany, University College, Ibadan, was elected first president, and Dr. Hopkins secretary. It is hoped that the next conference will be held in Zaria in December 1959.

Frederick Soddy Trust

The first report of the Frederick Soddy Trust (pp. 16. From the Frederick Soddy Trust, 9 The Drive, Hove 3, 1958) includes a full record of grants made up to September 1958 as well as a list of rejected applications, with the view of indicating the principles used in selection. Emphasis is placed on team-work rather than individual work, and on actual study and research in the field. Some details are given of the survey of crofting in South Uist and Benbecula made in 1957; of the proposed study of Corby and of a survey of the parish of Ardington, Berkshire, proposed by the University of Reading; and also of an expedition to the Pyrénées in which a study is to be made of peasant agriculture and its response to a mountain environment; an attempt is to be made to evaluate the extent of possible population movement in the area.

Smoke Control

Under the title "Smoke is Your Enemy" (pp. 8, 1959) the Ministry of Housing and Local Government and the Central Office of Information have prepared a short pamphlet for issue to householders in areas which local councils are proposing to make smoke control areas. The pamphlet explains simply what smoke control will mean to the household, the grants available to the householder and the advantages which smoke control will bring.

Exhibition of German Measuring Equipment

An exhibition of precision measuring equipment, made by Carl Zeiss (Oberkochen) and by M. Hensoldt and Soehne (Wetzlar) and mainly of interest to those working in the fields of engineering metrology and metallurgy, was held during March 9–14, in the showrooms of Degenhardt and Co., Ltd., at 6 Cavendish Square, London. Although the equipment displayed consisted mainly of new versions of well-known measuring and observing instruments, their new look made careful scrutiny necessary in some instances before identification with one or other of their famous prototypes could be made. In general, no claims were advanced for enhanced accuracy of performance over previous attainments, but outstanding improvements have been made in such matters as ease of manipulation of controls and adjustments. These new features considerably reduce the strain of continuous observing and contribute to the readier achievement by the user of the full potentialities of accuracy available in well-designed instruments. Ease of control was especially noticeable in the microscopes, of which the 'Ultraphot' camera microscope and the smaller Zeiss photomicroscope are typical examples; in addition, each is provided with a built-in automatic camera, and exposure time is regulated photoelectrically. The 'Technoscope', a binocular low-power microscope giving five different magnifications for the same working distance, has applications in the laboratory, the engineering workshop and the operating theatre. The range of engineering metrology equipment included the universal, tool-makers', interference and light-section microscopes, optical dividing heads, rotary dividing tables, alignment telescopes and a number of smaller measuring aids and devices.

Organization for European Economic Co-operation Courses on Nuclear Science

The European Nuclear Energy Agency of the Organization for European Economic Co-operation has arranged with the Atomic Energy Research Establishment at Harwell and the Centre d'Études Nucléaires at Saclay (France) for two international courses on nuclear energy. Designed for the teaching staffs of universities and higher technical colleges, each course will accept about fifty applicants, who will have the opportunity to study the latest advances in nuclear science and techniques, to do certain practical work, and to visit nuclear installations. The costs of these courses, both of which will run during July 20–31, are being borne by the European Nuclear Energy Agency, and participants will only be required to pay travel and living expenses.

The Night Sky in May

New moon occurs on May 7d. 20h. 11m. U.T. and full moon on May 22d. 12h. 56m. The following conjunctions with the Moon take place: May 11d. 14h., Venus 7° N.; May 13d. 03h., Mars 7° N.; May 22d. 06h., Jupiter 3° S.; May 24d. 21h., Saturn 4° S. In addition to these conjunctions with the Moon, Mars is in conjunction with Pollux on May 21d. 06h., Mars being 5·3° S., and Venus with Pollux on May 31d. 18h., Venus being 4·2° S. Mercury is too close to the Sun for observation. Venus is an evening star, visible in the south-west after sunset. Conditions are very favourable for observation. Venus sets at 23h. 00m., 23h. 20m. and 23h. 25m. on May 1, 15 and 31, respectively; its stellar magnitude is −3·7. Its distance decreases during the month from 104 to 82 million miles and the visible portion of the disk decreases from 0·734 to 0·607. Mars is moving eastwards among the stars and is in Gemini during May. It sets at 0h. 40m., 0h. 10m. and 23h. 35m. at the beginning, middle and end of the month, respectively. Its stellar magnitude decreases from +1·6 to +1·9 during the month, its distance from the Earth increasing from 173 to 197 million miles. Jupiter rises at 21h. 00m., 19h. 55m. and 18h. 30m. on May 1, 15 and 31, respectively, setting at 5h. 35m., 4h. 35m. and 3h. 20m. It is in Libra. The stellar magnitude of Jupiter is −2·1; its distance from the Earth on May 15 is approximately 410 million miles. Saturn is in Sagittarius, rising at 0h. 00m., 23h. 05m. and 21h. 55m. at the beginning, middle and end of the month, respectively. Its stellar magnitude is +0·5 and its distance approximately 870 million miles. The only occultation of a star brighter than magnitude 6 is that of 115 Tau, on May 10d. 20h. 08·3m. (disappearance at Greenwich).

Announcements

Lord Rothschild is joining the Board of 'Shell' Research, Ltd., on May 1 as part-time adviser on research. He is an assistant director of research in the Department of Zoology, University of Cambridge; until recently, he was chairman of the Agricultural Research Council, a post he occupied for ten years.

Dr. Walter R. Beam, manager of microwave advanced development in the Electron Tube Division of the Radio Corporation of America, has been appointed head of the Department of Electrical Engineering at Rensselaer Polytechnic Institute, Troy, New York.

An English translation of the *Astronomical Journal of the Academy of Sciences, U.S.S.R.*, issued in six parts annually, is being published by the American Institute of Physics in co-operation with the National Science Foundation, under the title *Soviet Astronomy —AJ*. The annual subscription is 25 dollars in the United States, or 27 dollars elsewhere, with special rates for university libraries. Orders and inquiries should be addressed to Translation Journals—*AJ*, 335 East 45 Street, New York 17.

The Glasshouse Crops Research Institute, Worthing Road, Rustington, Littlehampton, Sussex, will hold an open day on June 10. Particulars can be obtained from the Secretary of the Institute.

A conference on the Electric Arc in Welding will be held at the University of Birmingham on June 25. Further information can be obtained from the Secretary, Department of Industrial Metallurgy, University of Birmingham, Edgbaston, Birmingham 15.

An exhibition to commemorate the centenary of the death of Isambard Kingdom Brunel will be held in the main entrance hall of the Engineering Laboratory, Trumpington Street, Cambridge, during May 18–June 19, from 9 a.m. to 5 p.m. on weekdays and 9 a.m. to 12 noon on Saturdays. The exhibition will consist mainly of drawings and photographs of Brunel's principal works.

An exhibition of photometric instruments and microscopes applicable to most industrial processes and almost every branch of medicine, science and research will be held during May 11–21 in ~~the show~~rooms of Degenhardt and Co., Ltd., United Kingdom agents for Carl Zeiss, at 6 Cavendish Square, London, W.1. Throughout the exhibition four technical experts from the Zeiss works at Oberkochen will be in attendance to give advice on the applications of the instruments.

The Editorial Board of the *Journal of Embryology and Experimental Morphology* is sponsoring the fourth of its series of International Embryological Conferences at the Collège de France, Paris, during September 21–24. Details of its organization and scientific programme will be available on June 1 and can then be obtained from Prof. E. Wolff, Laboratoire d'Embryologie Experimentale, 49*bis* Avenue de la Belle Gabrielle, Nogent-sur-Marne, France, or from Dr. L. Brent, Department of Zoology, University College, Gower Street, London, W.C.1, England.

The 1959 conference of the Operational Research Society will be held at the Old Swan Hotel, Harrogate, during June 10–12. The fee is £15. The object of the conference is to provide an opportunity to explore and discuss possible directions for the future development of operational research, particularly in the fields of communications and decision making. Copies of the programme and application forms can be obtained from the Secretary, Operational Research Society, 64 Cannon Street, London, E.C.4.

The fourth International Conference on Ionization Phenomena in Gases will be held in Uppsala, Sweden, during August 17–21. The conference is being arranged by the University of Uppsala in collaboration with the Swedish National Committee for Physics. The main subjects will be: 1, fundamental processes in gas discharges; 2, high-frequency discharges; 3, glow discharges; 4, arc discharges; 5, spark discharges; 6, high-temperature plasmas and controlled fusion; 7, instabilities and oscillations in gas discharges; 8, new methods of measurements. Abstracts, not longer than 350 words, should be received by June 15. Further information can be obtained from the secretary general, Dr. Åke Nilsson, Institute of Physics, Uppsala.

THE COMMONWEALTH ADVISORY COMMITTEE ON DEFENCE SCIENCE

MEETING IN AUSTRALIA

THE Commonwealth Advisory Committee on Defence Science exists to develop the mutual interest of the countries of the British Commonwealth in defence science. Formal meetings are held at two- to three-year intervals in various member countries. Continuity is given to the work, between meetings, by a permanent Working Party located in London. The Working Party is made up of permanent representatives of member countries and is concerned with reviewing progress and planning for future meetings.

To date, five official meetings have been held in addition to a preliminary informal meeting which was held in 1946. Two of the formal meetings have been held in London, one in India, one in Canada and one recently in Australia.

Meetings are attended by senior officers from the Fighting Services and the Defence Scientific Services of the member countries, and it is an indication of the importance attached to the meetings that officers of the highest status are nominated as delegates.

Credit for the creation of the Commonwealth Advisory Committee on Defence Science rests largely with Sir Henry Tizard, who held a prominent position in defence science in the United Kingdom during the post-war period. One of the first acts of the meeting held recently in Australia was to send him a cable of greeting.

In proposing the preliminary or informal Conference which was held in 1946, the United Kingdom authorities suggested that the Conference might consider the distribution of defence research activities throughout the British Commonwealth so as to make the best possible use of the available and potential facilities and staff in each country. This has continued to be a goal for succeeding Conferences.

One of the decisions of the preliminary meeting in 1946 was that there should be close collaboration with the United States of America in the work of the Committee. Its constitution as a Commonwealth body precluded the United States from becoming a member; but a close association has been maintained, and at all meetings of the Committee American observers have been present by invitation and have made significant contributions to the discussions.

The fifth official meeting of the Committee was held in Australia during the period of October 7–28. It was attended by some sixty delegates, approximately forty of whom were from overseas. Countries represented were Australia, Canada, India, New Zealand, Pakistan, South Africa and the United Kingdom, and in addition, a party of observers from the United States of America attended.

On this occasion Ceylon, the Federation of Rhodesia and Nyasaland, Ghana and Malaya were unable to be represented but are being kept informed of the Conference discussions.

On this occasion the general chairman of the meeting was Sir Leslie Martin, defence scientific adviser and chairman of the Defence Research and Development Policy Committee in Australia. Delegations, which were comprised of senior representatives of the Fighting Services and the Defence Scientific Services of the member countries, were led by: Australia, Mr. W. A. S. Butement, chief scientist, Department of Supply; Canada, Dr. J. L. Keyston, vice-chairman, Defence Research Board; India, Brigadier Y. B. Gulati, director of weapons and equipment, Army Headquarters; New Zealand, Dr. C. D. Ellyett, Defence Science Advisers Committee; Pakistan, Dr. Mohammed Afaf, senior scientific officer, Defence Ministry; South Africa, Dr. S. Biesheuval, director, National Institute for Personnel Research; United Kingdom, Sir John Carroll, deputy controller, Research and Development, Admiralty; United States (observers), Mr. J. B. Macaulay, deputy assistant secretary, Research and Engineering, Department of Defense.

In planning the meeting, it was considered important that while full opportunity should be given for adequate Conference discussions, there should also be the opportunity for delegates to obtain a broad picture of defence science activities in Australia. This would also provide the occasion to see something of the geography and general development of the country.

To achieve these objectives, the itinerary provided for arrival of delegates in Sydney, the official opening in Canberra, the main business sessions to be held in Melbourne and Adelaide and for visits to be made to places of scientific service and general interest. This itinerary involved some 3,000 miles travel by air and, therefore, introduced problems of organization, but the results were such that the effort was considered well worth while.

The Conference was opened by the Prime Minister of Australia, the Hon. R. G. Menzies, in Canberra on October 7. In his address, Mr. Menzies directed attention to two points which were important in relation to the social implications of defence science. He commented that, because of the glamour attached to the subject at the present time, there was a tendency for the public to think of defence science as being concerned solely with new and revolutionary developments of a most complex character. While much of the work was, of course, of this nature, he as a layman was most impressed in studying the Conference agenda to find that there was still a great deal of research to be carried out on such everyday items as food, clothing and the weather.

The other point which Mr. Menzies commended to delegates was that defence science was being presented to the public in a way which caused them to feel that these very great efforts were being made solely for military purposes and were, therefore, very largely of a destructive character. He considered that this was far from the truth, and he was of the opinion that there were few defence scientific developments of recent years where the potential application for civil purposes was not of far greater importance than the military application.

The agenda was made up of some seventy technical papers in addition to the reports of the subcommittees on Service psychology and defence food research and the group on agricultural aspects of defence science. The papers were circulated in advance, and at the Conference they were introduced briefly by named delegates and then discussed by the whole meeting. The papers fell largely in the broad fields covered by the above groups and in the fields of career development, telecommunications, tropical warfare, weapons testing, naval research cold-weather operations, effects of high-level noise and the effects of nuclear weapons. However, in addition, there were many individual papers outside these groups.

The subject of tropical warfare was one of special interest to several of the countries represented, in that their territories embraced large areas of tropical terrain. Numerous papers were discussed, ranging from the effect of the environment on the soldier and his equipment, the need for more efficient vehicles and aircraft for use in tropical areas, mental stress under tropical conditions, navigation and communication in the jungle, clearance of vegetation, corrosion in the tropics, etc.

The weapons-testing theme covered the biggest group of papers discussed at the Conference. The subject was interpreted in its broadest sense, aeroplanes, for example, being treated as weapons. This theme was of great interest to Australia, where two of the major defence science activities, namely, the Woomera Missile Testing Range and the Maralinga Atomic Testing Range, are both concerned very largely with the testing of weapons.

In particular, the Woomera project was discussed in some detail. Numerous papers dealing with the equipment of the Range, various aspects of the trials work and the processing of the results were considered. The discussions were supplemented by a comprehensive visit to Woomera, when the facilities were examined in detail and missile trials were witnessed.

While at Woomera, delegates inspected the missile-tracking station which had been established as part of the International Geophysical Year programme.

The visit to Woomera was of particular interest to delegates. The basic conception of this project arose largely from the early discussions by the Commonwealth Advisory Committee on Defence Science, and it was a matter of considerable satisfaction to delegates to see the very tangible result that had been produced. Sir John Carroll, leader of the British delegation, in a public address, referred to Woomera as the outstanding example of defence science co-operation in the Free World.

Because of the importance attached to seeing at first hand something of the scientific work proceeding in Australia, several visits were arranged to scientific and appropriate Service establishments. Included in these were the Aeronautical Research Laboratories, the Defence Standards Laboratories, the Weapons Research Establishments at Salisbury and the testing range at Woomera, the Maralinga Atomic Testing Establishments and the Edinburgh and Woomera Royal Air Force Establishments.

Quite apart from these visits, it was felt that it would be of interest for delegates to be given opportunities of seeing something of the country and of work proceeding in other technical fields. For this purpose, a two-day visit was arranged to the Snowy Mountains Scheme in the south-eastern corner of Australia. This is the largest engineering undertaking in Australia, and can compare in magnitude with the largest undertakings in other parts of the world. Although primarily concerned with the conservation of water by means of river diversion and large-scale storage, it is also a major generator of electric power, having a potential capacity of some 2,000,000 kW.

Numerous opportunities were included in the programme to enable delegates to meet Australians in many walks of life. Delegates were honoured by being entertained to lunch by the Government of the Commonwealth and by being received by the Governors of Victoria and South Australia and by the Lord Mayor of Melbourne. In addition to such official functions, several pleasant informal functions including visits to places of interest and private entertainments were arranged—visits to outback sheep stations and to the Andamooka opal fields.

At the close of the Conference, delegates were unanimous that it was one of the most successful held to date. The tangible results are, of course, a series of recommendations arising from three weeks of intensive discussions. These recommendations are for the guidance of member countries; they will be submitted to the respective governments for ratification, when they will become a valuable guide to defence science policies. The other result of the Conference is the intangible one arising from the friendships established between delegates and the mutual appreciation of the special problems faced by member countries.

LESLIE MARTIN

AUTOMATIC REDUCTION OF GEOPHYSICAL DATA

OVER the past two decades there has been a rapid increase in the use of automatic photographic and electronic techniques for recording experimental results. As a result, the number of measurements made need no longer be restricted by fatigue in the experimenter, and sets of results containing millions of measurements are not uncommon. The rate at which results can be accumulated is now so great that the individuals responsible for setting up the equipment can no longer assimilate the information at the rate at which it is produced. This problem can be overcome to some extent by arranging the programme of analysis in such a way that the reduction of data can be dealt with by semi-skilled staff.

Nowadays even this solution is often inadequate. Not only is it difficult to find suitable staff, but also many of the investigations require the analysis of data on a scale so great as to be beyond the capabilities of a team of individuals. The problem is particularly acute in the field of geophysical research, where very large quantities of results are frequently produced in the course of field work of many kinds.

The automatic reduction of geophysical data was the subject of a Geophysical Discussion organized by the Royal Astronomical Society and held on January 23 under the chairmanship of Sir Edward Bullard. Although the discussion was not primarily concerned with the results of the International Geophysical Year, it was appropriate that it should have been arranged at a time when many individuals must be giving consideration to the study of the unprecedented wealth of new information obtained during the preceding eighteen months.

Sir Edward opened the discussion by pointing out that a single measurement made in each degree square of the Earth's surface would amount to a total of nearly 70,000 readings, and that facilities for handling large numbers of data are almost essential in many types of geophysical work. Even in mobile experiments it was most desirable to arrange, if at all possible, for the results to be recorded directly in digital form. This saved a great deal of time later, since it avoided the need for manual punching on tape or cards, and it frequently made it possible to record data at a rate which would not be possible by other methods.

Sir Edward described his recent voyage in *Discovery II*, in the course of which 90,000 magnetic readings were made near the Azores. The results were recorded directly on punched tape together with other essential information which would be needed during the reduction stage. These included the date, time, records of clock adjustments and range changes and also the ship's position and heading. The programme for the computer was written in such a way that the whole reduction process could be dealt with in one stage. As the principal objective of the work was the study of small irregularities in the Earth's field, it was arranged that the regular component of the field should be removed as part of the computer programme.

Mr. R. H. Merson (Royal Aircraft Establishment) described some investigations of the orbits of artificial Earth satellites. The original aim of the work was to predict the times of future transits in order to enable more accurate positional data to be recorded. Later, it was found possible to gain valuable geodetic information from the results. The approximate size and shape of the orbit are first determined on a desk calculator. This orbit is then adjusted by successive approximations, using a digital computer, to give a least-squares fit with all the available observational information.

The accuracy of the observations is such that it has been possible to derive new values for the coefficients J and D in Jeffreys's expression for the Earth's gravitational potential and to make deductions concerning atmospheric drag on satellites.

The prediction of future transits of Earth satellites requires the rapid processing of incoming data if the results are to be produced in time to be of use. The conditions under which weather forecasts are produced are similar and provide an obvious reason for the use of a digital computer. Mr. G. A. Corby (Meteorological Office) discussed preliminary tests on the preparation of numerical forecasts with the aid of a computer. Barometric pressure and wind-speed measurements are received on tape in a variety of codes at a rate of about 100,000 a day and, to save time, the incoming tapes are decoded in the computer before being used for further processing. The object is to construct a contour map, showing the height of a constant-pressure surface over Europe and the North Atlantic, which accurately represents the observational data. In the least-squares fitting process, it is necessary to minimize the differences between the observed and calculated values of both pressure and wind speed. An additional requirement is that in the determination of the contours for any area, maximum weight must be given to the data from the nearest weather stations. The speed and accuracy with which the forecasts can be produced by automatic methods are satisfactory even though the techniques are still in the development stage.

Mr. M. H. P. Bott (University of Durham) discussed the use of a digital computer for determining the extent of geological formations from surface gravity anomalies. The anomaly due to a model consisting of a series of vertical rectangular prisms of arbitrary depth has been calculated. In the study of a particular formation the procedure adopted is to define a model which leads to the same calculated anomaly as that observed in the area under investigation. Providing the density of the formation is known, the form of the lower surface can be determined uniquely by this method. The technique has been successfully used on the Triassic rocks in Dumfries.

Dr. D. C. Martin (Royal Society) outlined briefly the arrangements which had been made for the collection of data during the International Geophysical Year. Full sets of data would be held in World Data Centres and selected data would be published in Annals of the International Geophysical Year. Although no plans had been made in advance for the automatic processing of the whole of these data, it seemed likely that much of the information would eventually be dealt with by machine methods.

Mr. M. J. Tucker (National Institute of Oceanography) discussed various techniques used in the spectral analysis of geophysical time-series with particular reference to the study of sea waves. Although the analysis can be carried out by deriving the Fourier components of the wave motion, it is often more satisfactory to express the results in terms of the power spectrum or the autocorrelation function.

Proposals for the application of a digital computer to the forecasting of the future behaviour of the ionosphere were outlined by Mr. C. M. Minnis (Radio Research Station). Present intentions are to represent the characteristics of the $F2$-layer in terms of a family of linear functions of solar activity based on all the past observational data. This can be achieved to a satisfactory degree of accuracy if an ionospheric index is used to represent solar activity. The intercepts and slopes which define the linear relations would be stored in a digital computer and those needed to make a forecast for a specified location, season, time of day and level of solar activity would be selected and used in conjunction with other data, in the later stages of the calculations. It is hoped that by this means it will be possible to make forecasts of a more practically useful type than those made using standard manual methods.

In many types of geophysical investigation the use of an automatic digital computer is almost essential if accurate results are to be produced quickly, but it must not be assumed that this is always so. Three speakers referred to work which was being carried out successfully and economically by other methods.

Mr. A. Dennison (British Petroleum Company) described the echo method for the exploration of underground geological formations and the difficulties associated with the usual 'single spot' method of recording the results. Variable-density and variable-area recording had also been tried and the resulting records, when suitably displayed, could give a striking visual picture of the density variations in the underlying structures without any of the computations normally associated with echo soundings.

The analysis of Earth tide records obtained using Milne–Shaw pendulums was explained by Mr. G. W. Lennon (Liverpool Observatory and Tidal Institute), who enumerated reasons why a digital computer would not be appropriate in this type of work. For example, the removal of spurious diurnal and semi-diurnal oscillations would be difficult to programme for a computer, quite apart from the impossibility of producing long records without discontinuities.

Finally, Mr. H. M. Iyer (National Institute of Oceanography) referred to the lack of interest in the study of microseisms. If properly analysed they could yield useful information, and Mr. Iyer described experimental equipment which had recently been developed for the automatic recording of several statistical characteristics of microseisms.

C. M. MINNIS

CHEMISTRY OF CONDENSED TANNINS

THE Plant Phenolics Group held a meeting on "The Chemistry of Condensed Tannins" at Queen Elizabeth College, University of London, on January 6 under the chairmanship of Prof. R. D. Haworth (University of Sheffield). More than sixty members and guests were present.

In the opening paper on "Acid-catalysed Polymerization of Phenolic Compounds", Dr. B. R. Brown (Oxford) briefly summarized past work on this subject and indicated a possible reaction mechanism. *p*-Methoxybenzyl alcohols condense with phenols preferentially in a position *para* to a hydroxyl group to yield diphenylmethanes. A suitably substituted flavan, for example 4′-methoxyflavan, undergoes this condensation via ring-fission. Condensation of 4′-methoxyflavan with 7-hydroxyflavan yields a compound containing two flavan units the structure of which is based upon the known *para*-orientation of these reactions.

The importance of flavan-3 : 4-diols in tannin chemistry has led to an investigation of flavan-4-ol, which condenses with phenols, and with 7-hydroxyflavan yields a flavan 'dimer' isolated as the crystalline acetate.

These condensations, like the acid-polymerization of catechin, require high acid concentrations and it is unlikely that they are involved in the conversion of catechins into tannins in plants. This work aims at establishing the structural details of this condensation and at producing 'polymers' of known structure which can be used for the trial of new degradative methods, which may also be valuable for the degradation of condensed tannins.

Dr. D. E. Hathway (British Leather Manufacturers' Research Association), in a paper entitled "Oxidative Polymerization Mechanisms for Catechins", first briefly reviewed the chemistry of the oxidation of *o*- and *p*-dihydroxy- and *vic*-trihydroxyphenols, which he illustrated by reference to the synthesis of the mould metabolite atromentin, to the formation of purpurogallin and the synthetic melanins, and to the transformation of gallates into ellagates. Possible mechanisms for the oxidation of coniferyl alcohol by laccase, and their relevance to lignin and lignan formation were also discussed.

Studies on the oxidation of (+)-catechin in aqueous and non-aqueous media and on the autoxidation of flavans related to catechin confirm that autoxidation of catechin to a polymer (catechin–tannin) proceeds via the corresponding *o*-quinone followed by intermolecular C—C linkage. The evidence suggests that the most likely linkage is between the 8-carbon of one molecule and the 6′-carbon of the second. The isolation, albeit in small yield, of *m*-hemipinic acid by oxidative degradation of the methylated reduced polymer substantiates this supposition. Further confirmation for the presence of head-to-tail units in the polymer was obtained from a study of the autoxidation and the enzymic oxidation of mixed substrates which resemble the head and tail of (+)-catechin. Enzymic oxidation by mushroom, potato and tobacco polyphenoloxidases proceeds at a faster rate and lower temperature than the autoxidation of catechin, and gives a product precisely similar to the autoxidation polymer.

The heartwood of *Acacia catechu* and the leaves of *Uncaria gambir* contain considerable quantities of (−)-*epi*catechin and (+)-catechin, respectively. The isolation, therefore, of purified tanning fractions in good yield from these sources, with properties similar to the autoxidation and enzymic oxidation polymers of catechin, strongly suggests that these tannins are formed from *epi*catechin and catechin, respectively, by the above mechanism.

Studies on the formation of oak-bark tannin indicate that (+)-catechin, (+)-gallocatechin and leucodelphinidin, which are formed in the leaves, are translocated via the sieve-tube system of the phloem to the cambium, where preferential enzymic oxidation of the pyrogallol phenols occurs. The resulting tail-to-tail polymer is stored in the bark. The remaining tannin action of the bark can be attributed to the occurrence of complex leucoanthocyanins.

In a paper on "Oxidative Condensation in Tea Fermentation", Dr. E. A. H. Roberts (Indian Tea Association) said that, according to Hathway and Seakins, oxidation of (+)-catechin is followed by a condensation between the catechol-*o*-quinone group of one molecule and the phloroglucinol ring of another. If phloroglucinol is added to an enzyme–catechol system, different intermediate- and end-products are formed, indicating a condensation of *o*-benzoquinone with highly active phloroglucinol. Oxidation of pyrogallol to purpurogallin, however, is not affected by the presence of phloroglucinol, which illustrates the very high reactivity associated with the hydroxy-*o*-benzoquinone system. Enzymic oxidations of (−)-*epi*gallocatechin and its gallate are similarly unaffected by the addition of phloroglucinol, but the addition of pyrogallol to these systems yields derivatives of purpurogallin (flavanotropolones). These observations suggest that, following oxidation of the gallocatechins, a condensation takes place between the pyrogallol groups of two separate molecules.

Gallic acid and pyrogallol will not condense to form purpurogallincarboxylic acid unless both substances are oxidized, and this suggests that in the gallocatechin series the condensation takes place between two oxidized molecules. This is supported by the results of a study of the conditions required for the formation of purpurogallin.

The oxidations of (−)-*epi*gallocatechin and its gallate are followed by a linkage of two molecules of the resultant *o*-quinones to form the *o*-quinone of a bisflavanol with the two pyrogallol groups joined by a C—C linkage. Further condensations of this type are excluded on steric grounds, and it is suggested that the primary condensation products undergo either oxidation or reduction. Reduction leads to the formation of one of three possible bisflavanols, whereas oxidation, if a galloyl group is present, could lead to the formation of one of two purpurogallin derivatives. The available evidence supports the view that the theaflavins of black tea have these structures.

Prof. K. Freudenberg (Heidelberg) said that the term leucoanthocyani(di)n was a misnomer for those naturally occuring substances which on treatment with hot mineral acid either under aerobic or anaerobic conditions yield anthocyanidins. He proposed that they be named either 'pre- or pro-anthocyanins'.

Dr. T. Swain (Low Temperature Research Station, Cambridge), in introducing his paper on "Methods for the Investigation of Complex Leucoanthocyanins", also referred to the confusion in the nomenclature of leucoanthocyanins. He suggested that leucoanthocyanins of known structure be called by their systematic name, whereas polymers and co-polymers of hydroxyflavans ('flavols') be known as 'flavolans'. Those flavolans which yielded anthocyanidins on treatment with hot mineral acid would be known as 'flavylogens'. Dr. Swain then described methods for separating polymeric leucoanthocyanins into size groups and for analysis of their end groups.

Mr. W. E. Hillis (Division of Forest Products, Commonwealth Scientific and Industrial Research Organization, Australia), in his paper on the formation of condensed tannins in plants (read by Dr. E. C. Bate-Smith), recalled the probable role of shikimic acid and related alicyclic acids in the biosynthesis of polyphenols. Shikimic acid is present in appreciable quantities in the actively proliferating cambium of eucalypts. A linear relation exists between the amounts of shikimic acid and the weights of enlarging leaves of young *Eucalyptus sieberiana* trees, but this relationship does not hold for the fully-grown leaf; later the amount of shikimic acid in mature leaves diminishes with age. The final stages of the biosynthesis of shikimic acid can occur in the dark, and therefore shikimic acid present elsewhere in the tree need not necessarily originate in the leaves. The distribution of shikimic acid in leaves differs from that of the soluble polyphenols.

Comparative studies of the polyphenols in the cambium, sapwood and heartwood of three *Eucalyptus* species revealed the same general pattern of polyphenols, but shikimic acid was absent from the heartwood and only traces occurred in the developing sapwood. Catechin was less in the heartwood, whereas ellagic and gallic acids increased. On the basis of these facts a possible scheme for the biosynthesis of the heartwood polyphenols was outlined.

Mr. Hillis recalled that he had previously suggested (Society of Leather Trades Chemists Symposium on Vegetable Tannins, 1956, p. 127) that as certain tannins contain appreciable amounts of polymeric leucoanthocyanins, monomeric forms, originating in the leaves, could be the precursors of these substances. Present information, however, favours the formation of heartwood leucoanthocyanins *in situ*. Adaptation of the leucoanthocyanin reaction has enabled the distribution of leucoanthocyanins in plant tissues to be studied by means of coloured photomicrographs.

In dealing with flavans of the resorcinol series in relation to the chemistry of commercially important condensed tannins, Dr. D. G. Roux (Leather Industries Research Institute, Grahamstown, South Africa) said that an examination of previous work on wattle and quebracho extracts indicated that no direct evidence had been provided for the occurrence of catechins or flavan-3 : 4-diols as basic units in the corresponding tannins. The stereochemistry of the recently isolated black wattle catechin (—)-3 : 7 : 3′ : 4′ : 5′-pentahydroxyflavan and (—)-7 : 3′ : 4′-trihydroxyflavan-3 : 4-diol of quebracho heartwood was discussed. The progress of condensation of these compounds in the wood was examined by anthocyanidin formation, by number average molecular weights and by tannin analyses on radial and vertical drillings. These methods afford possible biochemical evidence of the presence of leucoanthocyanidins as intact flavan-3 : 4-diol units in these condensed tannins. The mode of cross-linkage in these condensed tannins must allow for its labile nature.

The chairman encouraged a vigorous discussion at the end of each paper, and among those participating were Drs. White and King (Forestal Central Laboratories), Bate-Smith, Thompson and Whalley.

J. W. T. Seakins

BAMBOOS AND NUTMEGS

TWO important taxonomic studies have recently been published in *The Gardens' Bulletin* (Singapore, 16, 1958), namely, "Bamboos of Malaya" by R. E. Holttum, and "A Revision of the Malayan Myristicaceae" by J. Sinclair.

Holttum has pointed out that the classification of the bamboos, as of other Gramineae, is based on inflorescence, flower and fruit characters; and in so far as such work tends to be done in herbaria, remote from the tropical collecting grounds, much information that would be of great use to the field botanist fails to be included. In fact, what the field botanist mostly sees are bamboos not in flower. Hence the value of vegetative characters, in particular the culm-sheaths, in field observations. This, indeed, is the kind of information possessed by the Malays, by whom the many kinds of bamboo are put to manifold domestic and other uses. Accordingly, in the present very full and informative work, classifications based on both vegetative and reproductive characters are given, together with many excellent line drawings. Botanists and foresters will note with interest an observation on the flowering of bamboos in Malaya. In the equable climate which prevails there, the simultaneous, gregarious flowering of single species in particular areas, sometimes at intervals of several years, which is a well-known phenomenon in India, apparently does not occur. On the contrary, the native Malayan species can continue to grow indefinitely, flower sporadically from time to time, or in some instances, flowering a little almost continuously; the gregarious dying-back after a heavy flowering, as in India, is at most only an occasional feature of the Malayan scene. Among others, an item of considerable interest is a close analysis and comparison of the inflorescences in bamboos and grasses.

In revising the Myristicaceae, Sinclair has pointed out that a regional flora of this group, as, indeed, of any other group, is likely to be unsatisfactory unless it is seen against the considerably wider background of the species present in the whole of the adjacent Malaysian region. Thus, many species formerly considered to be confined to Malaya are now known to occur in Sumatra and Borneo. The difficulties encountered in the systematic treatment of the group are discussed. In the present revision, 53 species, 5 varieties and 1 form are described, whereas, in Ridley's "Flora", the equivalent numbers were 45 species and 4 varieties. Six new species are described. The text is well illustrated with line drawings and with photographs showing bark characters.

AMERICAN ARACHNIDA

The spider family Dictynidæ has only recently been separated from the allied Amaurobiidæ, and its North American species are here revised and described. It is a family of world-wide distribution, with more than thirty genera and three hundred species, predominantly found in the north temperate zone. A dozen are British.

The spiders themselves are small spinners of cribellate webs in a variety of situations, and are unusual in that many species are gregarious, living together in very large numbers. In some areas in the States their thick communal webs choke ornamental conifers and evergreens and so give the spiders an economic importance. Their general habits and mode of life are but little known, and of their courtship and mating even less has been described. As a whole they seem to belong to the spring and summer, at which season alone males are to be found. The females lay only a few eggs, enclosed in lenticular cocoons, which are hung in the webs.

A recent paper by Prof. R. V. Chamberlin and W. J. Gertsch* describes eight American genera and 159 species, 119 of which are placed in the genus Dictyna. All these are fully described with the close attention to detail that modern arachnology requires, and distribution maps are added for many of the commonest species. The paper ends with 47 plates, carrying more than 600 admirable drawings, the work of Miss Marjorie Statham, whose artistry has enriched so many recent publications from the American Museum of Natural History.

It is obvious that this is one of the most painstaking revisions of a family of spiders that has appeared in recent years, and the authors must be congratulated on their achievement. At the same time its true significance can be properly judged only if two other points are mentioned. The first is that the authors themselves describe the revision as "still in many ways a preliminary one", since very large collections of Dictynidæ are now held both in New York and Utah. Here is an indication of the amount of systematic work which even a single family of spiders may involve.

The second point is that this paper recalls others, comparable if not quite so large, lately published in the *Bulletin of the American Museum of Natural History*. Dr. Levi's revision of the genus Enoplognatha and Dr. Muma's survey of American Solpugida are conspicuous examples. These have been supplemented by the smaller but no less desirable publications in the lively series, now some two thousand in number, called *American Museum Novitates*. No fewer than twenty-six of these, all dealing with the systematic side of arachnology, have come into my laboratory during the past few years. Obviously, there is a vigorous and fertile school of arachnology in America, which is taking its share, and more, in the very considerable task of ordering the Arachnida of the world in a coherent, reliable and accurate system. Theodore Savory

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* *Bulletin of the American Museum of Natural History.* Vol. 116, Article 1: The Spider Family Dictynidae in America North of Mexico. By Prof. Ralph V. Chamberlin and Willis J. Gertsch. Pp. 1–152+plates 1–47. (New York: American Museum of Natural History, 1958.) 3.50 dollars.

OXYGEN AS A PREREQUISITE TO THE ORIGIN OF THE METAZOA

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During recent years there has been a revival of interest in the problems of the origin of life. This has led to speculation and experimentation, mostly along biochemical and biophysical lines. Less attention has been focused on the problems of the next steps in organic evolution, namely, those attending the diversification of primitive living forms into the kingdoms of organisms recognized to-day.

One of the important questions concerns the sudden appearance of highly organized metazoans in the fossil record. To state this more specifically: Why are there no fossil records of animal life from earlier periods than the Cambrian, the lower reaches of which are characterized by trilobites ? These are far too complex to have been the first animals that appeared on Earth, yet we have no traces of primitive ancestors to them. In Pre-Cambrian rocks there have been found some things that may be fossil sponge spicules and worm burrows, but that is about all. Various theories have been advanced to explain the lack of Pre-Cambrian fossils[1], but none is really satisfactory. However, the general intimation is that a long period of animal evolution must have occurred prior to the appearance of the trilobites, even although no traces remain. Recently Axelrod[2] postulated that the late Pre-Cambrian fauna might have developed in the littoral and immediate shore areas of the seas ; these areas are subject to rapid and drastic erosion, a circumstance which does not favour the fossilization and preservation of their inhabitants. Hence Pre-Cambrian fossils should be rare, but they ought to exist. Axelrod suggests that particular care be used in seeking Pre-Cambrian deposits that can be identified as having originated in shallow seas, and that careful examination be made for the fossil remains of microscopic animals.

I wish to suggest that the lack of faunal remains in Pre-Cambrian deposits indicates the non-existence of a metazoan fauna for the greatest part of that period. I agree with Cloud[3] that there was a rapid (tachytelic) diversification of metazoans in late Pre-Cambrian times, and with Axelrod that the early forms were probably minute. But I wish to argue that the rapid diversification and increase in numbers was brought about by one specific ecological change, namely, by the addition to the environment of a surplus of free oxygen. To support this point of view the following facts and considerations can be marshalled.

In Pre-Cambrian rocks, fossil algæ have been found which precipitated calcium carbonate about themselves in various manners. Of these, *Collenia* is the best-known genus. One supposed alga, *Corycium enigmaticum* Sederholm, is of Archæan age which, if the correlation cited by Rankama[4] is correct, makes the organism 900–1,200 million years old[5]. In addition to such named forms, sporadically occurring carbon deposits have been taken to indicate that life was present and abundant in some Pre-Cambrian times, although of what form or degree of development we do not know.

It is, I think, generally considered that the early atmosphere of the Earth was reducing. Molecular oxygen was foreign to the environment, having been used up in inorganic oxidations. Various chemical reactions have been proposed to explain the advent of oxygen in the atmosphere, but the activities of green plants seem to offer the best explanation of its presence.

The exciting advances made during the past couple of decades in the biochemistry of photosynthesis have demonstrated how chlorophyl molecules could have been built up from inorganic substances through organic substances such as glycine and succinic acid to protoporphyrins and finally complex porphyrin compounds[6]. Photosynthetic reactions could originate anærobically, with oxygen being produced through the photolysis of water.

I suggest the following steps as a possible sequence of events. The primitive forms of life were heterotrophes, absorbing as their nutrients organic substances dissolved in the seas in which they lived. These heterotrophes may have been of several origins and existed in various habitats. Their subsequent evolution would involve considerable 'experimentation' in efficiency of anærobic metabolism. The next step was the development of protochlorophylls by certain types of organisms which would allow the utilization of the energy of sunlight for the reduction of carbon dioxide and its fixation in the form of carbohydrates. The organisms with this ability had thus become autotrophic. If, as has been suggested by several authors, the dissolved organic substances of the seas were becoming depleted after millions of years of forage by heterotrophes, these autotrophes possessed a competitive advantage, namely, freedom from dependence on these substances. They spread rapidly throughout the seas of the Earth. With them went an increasing concentration of an excretory product, oxygen. Oxygen spread through the waters and, by diffusion, into the atmosphere above the waters.

The development of the autotrophes ensured the survival of some heterotrophes as predaceous or carrion-feeding forms. The specialization and spread of autotrophic forms took further millions of years as the process of photosynthesis was improved. This would be the period of development and deployment of algæ. During this time, supported by these plants, there also lived a nondescript assemblage of heterotrophes. The heterotrophes were probably extremely small, perhaps in the form of colloidal aggregates. Of these as yet there has been found no identifiable trace.

Not until the concentration of oxygen in the hydrosphere and atmosphere reached a level at which it became a constant part of the environment did it exert a significant effect on the evolution of the heterotrophes. That is to say, not until there was more than enough oxygen present to take care of the continuing demand of inorganic oxidations was there sufficient to enable organisms to utilize it metabolically. To reach this level of free oxygen required the passage of vast periods of time. Not until the late Pre-Cambrian was this condition reached, but once oxygen became a constant element in the environment, oxidative metabolism with its advantages rapidly became established. Both heterotrophes and autotrophes could partake of these advantages. A variety of primitive forms could respond to the altered environment by using the new, more efficient method of extracting energy from their food. The consequence of such metabolic improvement was the development of metazoan and metaphytic forms through tissue differentiation. It is interesting to note that the fossil record indicates that animals developed earlier into varieties of complex forms than did plants. This suggests that some environmental factor was of more immediate use to animals than to plants. Oxygen was just such a factor.

To summarize, I suggest that (1) the lack of Pre-Cambrian metazoan fossils can be explained primarily by the assumption that there were few metazoans to be fossilized ; (2) the addition of free oxygen to the environment as a constant feature only some 600 million years ago initiated a tachytelic development of metazoans (Urey gives 800 million years ago as the latest time to which a reducing atmosphere could have persisted[7]) ; but the amount of free oxygen required to initiate oxidative metabolism as a prerequisite of life may well have been much more than that required to enter inorganic reactions, so one can picture a period of, say, 200 million years during which there existed barely minimal conditions for partially oxidative life; (3) life spent 1,000 million years or more becoming organized anærobically in the pre-Cambrian seas. This stage ended about 600 million years ago when the concentration of free oxygen reached a level sufficiently high to make it a constant feature of the environment; this enabled some organisms to undertake oxidative metabolism. The subsequent abundance and diversity of metazoan life formed the fossil record as we know it.

I am indebted to Dr. Hans Kalmus for many stimulating and clarifying comments made during the time these ideas were being put in order.

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DEDUCTION OF IONOSPHERIC ELECTRON CONTENT FROM THE FARADAY FADING OF SIGNALS FROM ARTIFICIAL EARTH SATELLITES

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ONE of the most marked characteristics of the radio signals received from the Earth satellites has been the complex fading of the received signal. It is here shown that from a study of the fading it is possible to deduce the electron content for the sample of the ionosphere between the satellite and the receiving station for a large section of the observed trajectory. This gives a sample across the sky, and can give information about the region above the F_2 maximum which is unexplorable by the methods of ionospheric sounding.

These fadings fall into two classes; first, those due to a change in the energy flux at the receiving aerial; and secondly, those accompanying a rotation of the plane of polarization of this energy. These two classes may be distinguished by the comparison of the signals received simultaneously on three orthogonal dipoles. For the first class, the fades will be in phase for all aerials, whereas for the second class there will be relative phase shifts depending upon the direction of arrival of the signal with respect to the dipole axes.

For signals received on a dipole from a satellite moving on a trajectory above an ionized layer, there will be a fading due to the variation in the Faraday rotation of the plane of polarization and also a fading due to the spin of the satellite. It can be shown that the variation in Faraday rotation can arise because of changes in: (*a*) electron content between satellite and receiver; (*b*) intensity of the Earth's magnetic field; and (*c*) angle between this field and the path of the ray in the ionized region.

Hence the rate of fading observed for transits in or above the F-region will be that due to the change in Faraday rotation which may be unmodified, increased or decreased by twice the spin-frequency of the satellite. During many transits a sudden change of twice the spin-frequency was observed in the rate of fading when the reception geometry changed; such a change appears in Fig. 1.

In order to evaluate the electron content corresponding to any part of the trajectory, it is necessary to know the absolute number of rotations of the plane of polarization due to the Faraday effect, as the signal travels from satellite to receiver. In the case of a ray passing normal to the Earth's magnetic field in the ionosphere, the Faraday effect will be very small and to a first approximation may be equated to zero.

This condition will occur at two points on any transit of the satellite, but they may be beyond the observer's radio horizon. However, for observers in Britain and trajectories such as those of the Russian Earth satellites, one of these points may be above the observer's radio horizon when the satellite is at a low angle of elevation north of the observer. The angle of elevation of this point increases as the observer moves farther south towards the magnetic equator. When one of these points is near or above the radio horizon, it is possible to count the number of Faraday rotations of the received signal as the

Table 1

Transit date, time, G.M.T.	n_s (Faraday rotation)		Ionogram		Geomagnetic latitude	$(h_s - h_m F_2)$ km.
	Farnborough	Cambridge	n_s	n_T		
October 18, 1957 03.30		8·2	7·0	4·6	Slough (54°)	40
		5·5	4·8	3·9	Inverness (60°)	10
October 19, 1957 03.30	6·4	6·8	6·9	4·0	Slough	50
	2·8	2·9	3·5	3·5	Inverness	0
November 7, 1957 14.00	31·8	28·2	47·5	14·8	Slough	240
	15·5	16·5	16·5	9·4	Inverness	160

n_T is the number of electrons ($\times 10^{-12}$) in a cm.^{2} vertical column up to the height of F_2 maximum as deduced from ionograms; n_s is the number of electrons ($\times 10^{-12}$) in a cm.^{2} vertical column up to the height of the satellite.

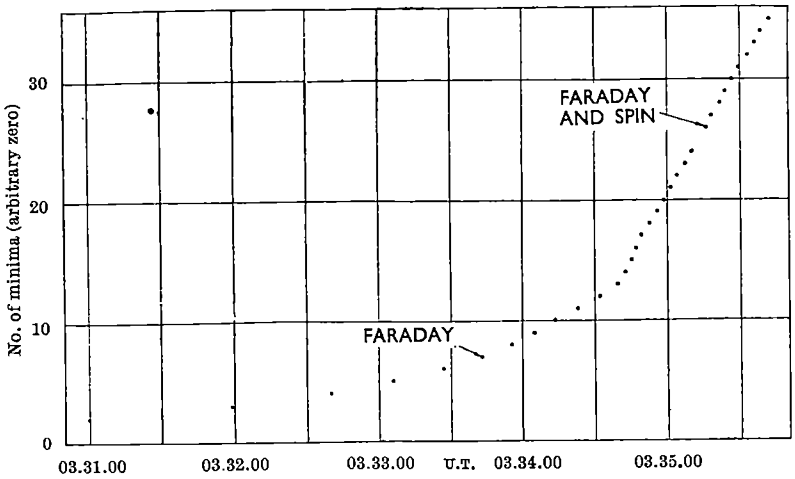

Fig. 1. No. of minima on the fading record taken on October 19, 1957. 40 Mc./s. signal

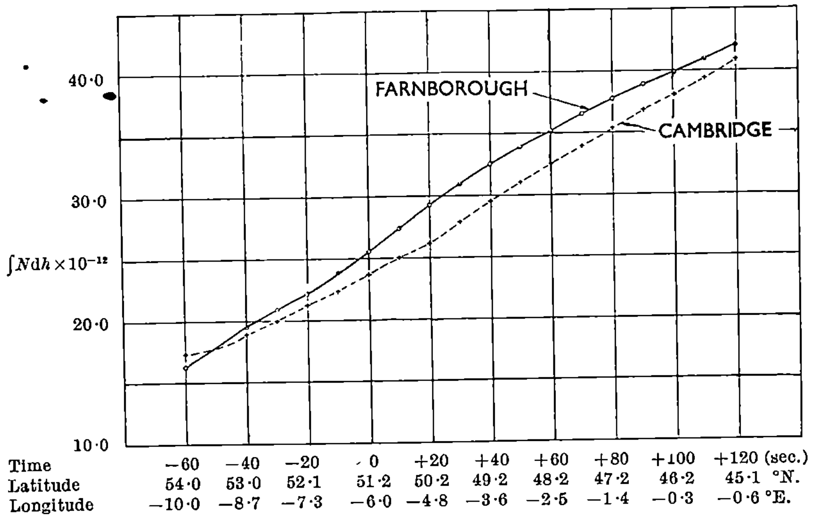

Fig. 2. $\int Ndh$ plotted as a function of position for Farnborough and Cambridge observations

satellite moves through this point to any point on the trajectory. From this number of rotations the electron content of that part of the ionosphere between observer and satellite can then be calculated for various points along the trajectory, and hence the variation of the electron content along a slice of the ionosphere can be determined.

This method has been used to interpret fading records of *Sputniks* 1 and 2 taken at Farnborough and Cambridge when the satellites were nearly overhead and at heights above the F_2 maximum of the ionosphere. The resulting values of electron content could be checked against those deduced from ionograms taken at Slough and Inverness. A comparison of the results is shown in Table 1.

On any one transit the satellite did not pass over both Inverness and Slough. The vertical-incidence results were therefore compared with observations when the satellite was at the corresponding geomagnetic latitude. Geomagnetic co-ordinates were chosen because the data for the critical frequency of the F_2-region over the Earth's surface correlate well with them[1]. Table 1 shows this comparison where n_s, Farnborough and Cambridge, relate to satellite observations, and n_s, Slough and Inverness, to vertical-incidence soundings. At Slough and Inverness n_s was estimated assuming a block of ionization of density NmF_2 extending from the height of the F_2 maximum (hmF_2) up to the heights of the satellite, h_s.

For the 03.30 transits of *Sputnik* 1 on October 18 and 19, 1957, the height of the satellite was only some 50 km. above hmF_2, and the estimated value of n_s (Slough and Inverness) should be only slightly larger than the values obtained from observations of the satellite. This conclusion is supported by the experimental results shown in Table 1. The slight discrepancies that arise can be attributed to errors in height of about 10 km. in either the satellite height or hmF_2.

In the case of the 14.00 transit of *Sputnik* 2 on November 7, 1957, the height of the satellite was well above hmF_2 (about 200 km.). The value of n_s obtained from the observations of the satellite would be expected to be markedly less than that deduced from the vertical-incidence soundings, assuming a block of ionization above hmF_2. The value of n_s (Slough) compared with the satellite observations made at Farnborough and Cambridge is consistent with the above view. In the case of this high transit, the ionosphere explored when the satellite was at the geomagnetic latitude of Inverness was a region south of this latitude. It is shown in Fig. 2 that the electron content decreases towards the north, so that the proper value of n_s (Farnborough and Cambridge), to compare with n_s (Inverness), should be smaller than the value given in Table 1. The satellite observations made on November 7 are therefore consistent with the vertical-incidence soundings.

A comparison of the values of electron content deduced from simultaneous observations made at Farnborough and Cambridge is shown in Fig. 2. At the ends of the transit where the ray paths would pass through the same part of the ionosphere on the way to either base, the measured values are in good agreement. The difference in values in mid-transit probably results from the fact that the rays to Farnborough and Cambridge then follow different paths, with the Cambridge path north of the Farnborough path.

The results presented here show good agreement for observations at different stations, and also agreement with estimates made by an independent method. We conclude, therefore, that the method of analysis is reliable, and further observations along these lines are in progress. The method provides a way of determining horizontal variations in the ionosphere both above and below the maximum of ionization, and has the advantages that the experimental technique and apparatus used are simple, while timing accuracy of about one or two seconds is sufficient.

In carrying out this work we have been helped greatly by the provision of ionograms from the Department of Scientific and Industrial Research stations at Slough and Inverness, and by the staff of the Cavendish Laboratory, who have computed total electron content from ionograms and most generously made available fading records to supplement those taken in our own Establishment. Acknowledgment is made to the Chief Scientist, Ministry of Supply, for permission to publish the communication.

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EFFECTS OF WAVE-LENGTH AND TIME OF IRRADIATION ON INTERNODE LENGTH IN *PISUM SATIVUM* AND *TROPAEOLUM MAJUS*

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THE relative effectiveness of red and blue radiation in controlling photomorphogenic responses of plants has been the subject of some disagreement. Workers at Beltsville have demonstrated a light reaction governing internode length, hypocotyl length, leaf expansion, seed germination, etc., which is mediated through a reversible red/infra-red system[1,2]. However, the effect of blue radiation is far from clear. Downs *et al.*[1], working with the second internode of *Phaseolus*, have claimed that supposed effects of blue radiation can be shown to be due to the relative levels of red and infra-red contamination in the source of blue light. For seed germination, however, an unequivocal effect of blue light, acting in the same direction as infra-red, has been demonstrated by Flint and McAlister[3]. Borthwick *et al.*[4] have suggested that both the infra-red and red-absorbing forms of the red/infra-red pigment have some absorption in the region 400–500 mμ, and that germination is promoted by blue light when the pigment is in the red-absorbing form and inhibited by blue light when the pigment is in the infra-red-absorbing form. The results of the Beltsville group have come mainly from short-term irradiation experiments with etiolated material of *Pisum*, *Phaseolus* and *Hordeum* grown in the dark. Workers in Europe have suggested that the relative effectiveness of blue and red radiation in determining final internode lengths varies according to the experimental technique, particularly the intensity of the light used and the duration of the illumination period[5]. Previous reports[6] from this laboratory have shown, however, that different results are obtainable when different species are given similar conditions of irradiation; shortest internodes occurred in red in *Pisum* and *Calendula*, and in blue in *Lycopersicon* and *Lactuca*. These relative differences in response held over a range of intensities, but very low intensities could not be used for the small-seeded 'blue-sensitive' species. However, the relatively large-seeded species *Tropaeolum majus* has been found to develop shorter internodes in blue than in red light and, accordingly, it has now been possible to measure the responses of the 'red sensitive' and 'blue sensitive' species over a much wider range of irradiances.

The plants used in the investigation were *Pisum sativum* Meteor and *Tropaeolum majus* Double Orange Gleam. The blue and red wave-bands isolated from coloured fluorescent lamps are those described previously[6]; the infra-red was obtained by filtering light from water-cooled 300-watt tungsten-filament lamps through a 1-cm. thickness of 0·1 per cent solution of naphthalene black in water. The wave-bands used are shown in Fig. 1. The red and blue sources were equated on the basis of equal incident quanta. Seedlings were grown at 21° C. and were irradiated from germination with times ranging from 15 min. to 24 hr. in each day. Measurements were made after 14 days; only fully elongated internodes were measured, that is, internodes 2 (first to second scale leaf), 3 and 4 in *Pisum* and internode 1 (soil to first node) in *Tropaeolum*. Results from two experiments at different energy-levels are presented in Fig. 2. The difference in the response of the two species is obvious. For short periods of irradiation red is the more effective in reducing internode extension in both species but, whereas in *Pisum* this effect is maintained for all times of irradiation, in *Tropaeolum* the relative effectiveness of red and blue radiation is reversed for times of irradiation of more than about 1½ hr.

In view of the red/infra-red system cited above, the effect of the near infra-red region on these responses was investigated. Times of irradiation of 4 hr. were chosen to bring the responses into the

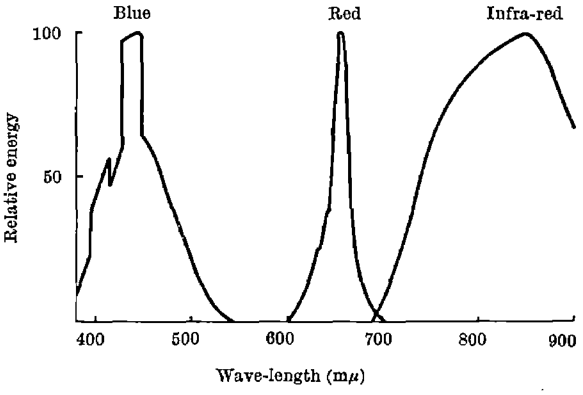

Fig. 1. Relative wave-length distribution of light sources

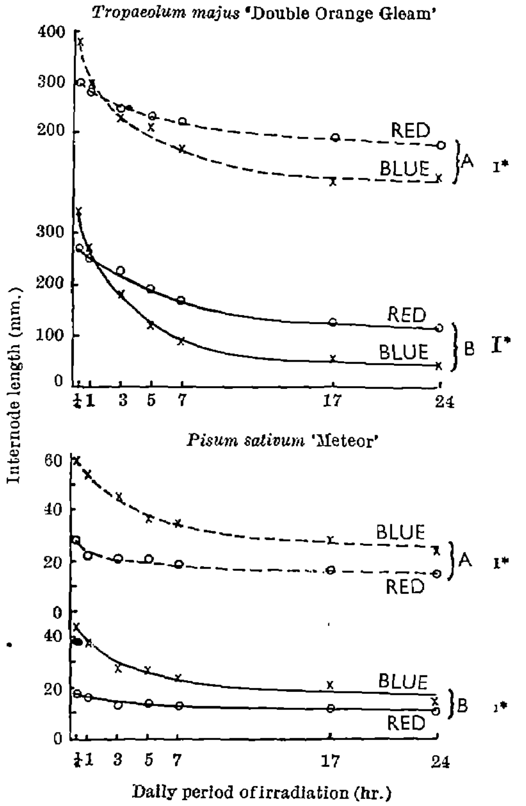

Fig. 2. Effect of irradiation on final internode length. Values for *Pisum* are means for internodes 2–4, for *Tropaeolum* are for internode 1 (see text)

(*A*) Energy-levels { Blue 900 ergs cm.$^{-2}$ sec.$^{-1}$; Red 900 × 0·68 ergs cm.$^{-2}$ sec.$^{-1}$ }
(*B*) Energy-levels × 5 those in (*A*)
Dark values: *Pisum* (*A*) 81·2 mm., and (*B*) 66·0 mm.; *Tropaeolum* (*A*) 556 mm., and (*B*) 593 mm.
* Significant difference at $P = 0{\cdot}05$

region of relatively greater blue effectiveness for *Tropaeolum*. The treatments listed in Table 1 were given every 24 hr. Fully expanded internodes were measured as before after 12 days and the results (mean of two experiments) are given in Table 1. Although differing in their response to blue or red light at these times of irradiation, the two species behaved in essentially the same manner with regard to the effects of one wave-band of irradiation on another. Preliminary treatment with infra-red did not affect the response to either blue or red radiation. The effect of red radiation was almost completely reversed by subsequent exposure to infra-red even with these rather long preliminary exposures to red, when some irreversible growth responses might be expected to have occurred (namely, 4 hr. compared with the usual exposure times to red of 2–5 min. in reversal experiments of this kind). The effect of blue radiation, on the other hand, was only slightly reduced by subsequent irradiation in the near infra-red.

Table 1

Irradiation treatments			Length* of fully expanded internode (mm.)	
4 hr.	4 hr.	16 hr.	*Pisum*†	*Tropaeolum*‡
Infra-red	Dark	Dark	54·0	295·4
Blue	Dark	Dark	27·7	135·5
Infra-red	Blue	Dark	26·4	125·0
Blue	Infra-red	Dark	35·1	156·5
Red	Dark	Dark	13·6	188·0
Infra-red	Red	Dark	15·7	173·5
Red	Infra-red	Dark	42·5	250·2
Blue	Red	Dark	12·5	84·3
Red	Blue	Dark	19·2	123·0
Blue	Blue	Dark	23·8	96·8
Red	Red	Dark	11·9	162·0
Significant difference at $P = 0{\cdot}05$			5·9	20·6

* Means from two experiments.
† Mean of internodes 2–4.
‡ Internode 1.

Energy-levels { blue, 5,650 ergs cm.$^{-2}$ sec.$^{-1}$; red, 5,650 × 0·68 ergs cm.$^{-2}$ sec.$^{-1}$; infra-red, 4,160 ergs cm.$^{-2}$ sec.$^{-1}$ }

The results presented are in accordance with the hypothesis that there are at least two photochemical reactions controlling internode expansion in these species. The preliminary low-intensity reaction (I) is the well-known red/infra-red reversible reaction established by the Beltsville workers. At longer times of irradiation in *Tropaeolum* a second system (II) becomes more important; this latter system is more sensitive to blue radiation and is not reversible by infra-red. The effects of these two reactions appear to be additive. The presence of the latter system in *Pisum* is indicated by the fact that, following exposure to blue, infra-red has relatively little effect; however, at all the times of irradiation used, internode elongation was more effectively suppressed in *Pisum* by red than by blue light.

The treatment blue–red (Table 1) is of interest since this treatment is more effective than red–blue in causing reduction in internode length, although quantitatively the treatments are the same. In *Tropaeolum*, blue–red is more effective than red–red or blue–blue; in *Pisum*, it is more effective than blue–blue and as effective as red–red. These results can be explained if we assume that, in addition to any effect in 'reaction II', some blue light in the region 400–500 mμ is absorbed by both forms of the red/infra-red reversible pigment, and that its action in this system will depend on whether the pigment is in the red- or infra-red-absorbing form at the start of the blue irradiation (as suggested for the promotion and inhibition of seed germination in lettuce by Borthwick *et al.*[4]). At the end of the 16-hr. dark period most of the red/infra-red pigment will be in the red-absorbing form. Then, in the blue–red treatment, during the blue irradiation there will be a positive effect in 'reaction II' and some of the red/infra-red pigment will be converted to the infra-red absorbing (that is, active form); the subsequent exposure to red will increase this conversion. Conversely, in the red–blue treatment, most of the pigment will be in the infra-red-absorbing form at the end of the irradiation with red light and subsequent exposure to blue will tend to reverse the red effect; there will, however, be a positive effect of blue in 'reaction II'. There is no measurable infra-red contamination present in the source of blue light used in these experiments.

Further experiments are in progress on the time/intensity reciprocity in these responses.

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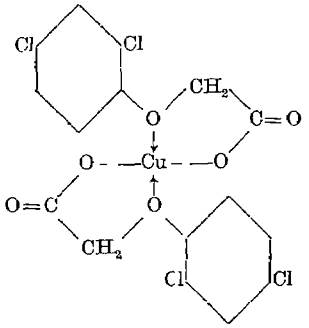
METAL-CHELATING PROPERTIES OF PLANT-GROWTH SUBSTANCES

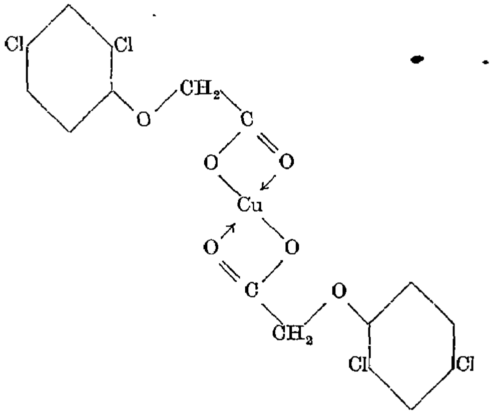
THE suggestion that plant-growth substances act by virtue of their ability to chelate metal ions has received some support from work reported recently by Cohen *et al.*[1] on the formation of copper complexes by indoleacetic acid and naphthalene-α-acetic acid. We wish to report experiments, prompted by their communication, which can be taken to contradict this general hypothesis and disagree in detail with some of the results quoted. We have formed and measured the stability constants of copper complexes of phenoxyacetic acids which have a wide range of growth activity. On the suggested hypothesis the copper complexes should show a similar wide range of stability constants, but we have found them to be indistinguishable.

The copper complexes of the following acids have been studied: 2 : 4-dimethylphenoxyacetic acid, 4-chloro-2-methyl phenoxyacetic acid and 2 : 4-dichlorophenoxyacetic acid, and the analyses of the complexes are shown in Table 1. We have also made measurements of the copper complex of naphthalene-α-acetic acid for comparison with earlier work. Attempts to obtain evidence of the formation of copper complexes in this series with an acid/copper ratio of 1 : 1 failed. The complexes isolated under various conditions were shown to be hydrates of the (2 : 1 : acid : copper) compounds. After dehydration at 140° C. and 0·1 mm., the anhydrous salts were quite stable and did not absorb moisture from the air even after standing for a week. The optical densities of 50 per cent ethanolic solutions containing increasing ratios of acid/copper were determined at wave-lengths where the copper complex absorbs relatively more than the free acids. Plots of optical density against the ratio of acid/copper showed only one break in the curve, at an acid/copper ratio of approximately 2.

Whether or not the materials described above are true complexes in which the organic component is doubly bound to the metal may be questioned. The alternative would be to regard them as simple copper salts. In view of the stability of the anhydrous materials, the formulation as salts would only be valid if the copper had a co-ordination number of 2. The usual co-ordination number of 4 would be consistent with complex formation, involving either one acid and one other oxygen atom as in I or the two acid oxygen atoms as in II. The latter structure has been established for the copper derivatives of fatty acids[2], and we regard it as likely also to be correct in the phenoxyacetic acid series.



(I)



(II)

The stability constants of the copper complexes were determined by pH titration measurements[3] in 50 per cent ethanol. The values in Table 2 were calculated from measurements made in the absence of a strong acid, following what was apparently done by Cohen *et al.*[1]. The *pKc* values differ very little and the copper complex of the acid with the least growth activity is the most stable. Our value for the *pKa* of naphthalene-α-acetic acid (5·76) differs from theirs (4·6), so that the calculated *pKc* which critically depends on the determined *pKa* is also different from their value of 5·4. In so far as our value is higher, it indicates a slightly greater stability for the complex. The presence of a strong acid, however, is theoretically important to the method of pH titration[4] and Table 3 lists the constants determined in 50 per cent ethanol in the presence of a strong acid (10^{-5} *M* nitric acid). It will be seen that the stability constants of the five copper complexes differ by insignificant amounts; indeed, the second figure is scarcely reliable, considering the assumptions made

Table 1

Copper complex	Found C	Found H	Formula for dehydrated complex	Calculated C	Calculated H	Hydrate	M.p. (°C.)
2 : 4-Dimethylphenoxyacetic acid	56·93	5·14	$C_{20}H_{22}O_6Cu$	56·94	5·26	$2 H_2O$	235–6 (decomp.)
2-Methyl-4-chlorophenoxyacetic acid	46·51	3·53	$C_{18}H_{16}O_6Cl_2Cu$	46·73	3·49	$2 H_2O$	247–9 (decomp.)
2 : 4-Dichlorophenoxyacetic acid	38·14	2·25	$C_{16}H_{10}O_6Cl_4Cu$	38·18	2·00	$5 H_2O$	254–6 (decomp.)

Table 2

Copper complex	Stability constants of copper complexes based on measurements in the absence of a strong acid			
	pKa	pK_1	pK_2	pKc
Naphthalene acetic acid	5·76	5·1	4·5	9·6
2 : 4-Dimethylphenoxyacetic acid	4·54	4·6	4·2	8·8
2-Methyl-4-chlorophenoxyacetic acid	4·36	4·3	4·0	8·3
2 : 4-Dichlorophenoxyacetic acid	4·20	4·3	3·8	8·1

pKa is the equilibrium constant of the acid; temperature, 21° C. (pK_1 and pK_2) = pKc, the chelate stability constant of the reaction: $2A^- + Cu^{++}\ (A)_2Cu$; all determinations made in 50 per cent ethanol.

Table 3

Copper complex	Stability constants of copper complexes based on measurements made in the presence of 10^{-5} *M* nitric acid				Growth activity of acid (dose in μgm. needed to give 50 per cent leaf repression)
	pKa	pK_1	pK_2	pKc	
Naphthalene-α-acetic acid	5·75*	5·2*	4·5*	9·7*	0·2±0·1
2 : 4-Dimethylphenoxy-acetic acid	4·53	4·6	3·9	8·5	28±2
2-Methyl-4-chlorophen-oxyacetic acid	4·39	4·4	3·8	8·2	0·15±0·02
2 : 4-Dichlorophenoxy-acetic acid	4·19	4·3	4·2	8·5	0·04±0·005

* Identical values obtained in independent experiments; temperature, 25° C.; all measurements in 50 per cent ethanol.

in calculating the *pKc*. Similar disagreement with the recorded *pKc* for indoleacetic acid – copper complex has been reported recently by Recaldin and Heath[5], although it is not clear what conditions were used for their measurement.

Parallel with the measurements of the stability of the copper complexes, we have made quantitative estimates of the growth-regulating activity of each of these growth substances by the method of Brown and Weintraub[6]. In the last column of Table 3 are listed the quantities of each acid required to depress the growth of the first trifoliate leaf of a *Phaseolus* seedling by 50 per cent. The percentage repression in this test is linearly related to the logarithm of the dose, and the figures for 50 per cent repression are inversely related to the growth activity. It will be seen that 2 : 4-chlorophenoxyacetic acid is almost a thousand-fold more active than dimethylphenoxyacetic acid, though its ability to bind copper is not measurably different.

We therefore suggest that in spite of some evidence in the literature for a relation between metal-complexing capacity and plant-growth activity, the properties by which certain molecules are specifically able to act as growth regulators still remain a mystery.

Our thanks are due to the directors of Imperial Chemical Industries of Australia and New Zealand for permission to publish this communication, and to Mr. D. Fieldhouse, Mrs. M. Markus and Mrs. V. Zangari for technical assistance.

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IN putting forward the hypothesis that plant-growth substances might act as such through their metal complex-forming activities[1,2] we did not suggest that no other properties of the molecules concerned could modify their effects upon growth. We specifically raised the question of rate of penetration, and in view of the very various growth-promoting activities of the different agents tried (a variation by no means parallel with their metal-complexing capacities) we had in mind the possibilities that steric hindrance or toxicity might also be modifying the amount of growth promotion obtained.

One might well hesitate to accept that the 'growth-regulating activity' of 2 : 4-dichlorophenoxyacetic acid is almost a thousand times as great as that of dimethylphenoxyacetic acid on the basis of an assay test depending on the inhibition of growth, such as that used by Armarego *et al.* (preceding communication), but other work[3] suggests that their growth-promoting activities in the *Avena* cylinder test are in a similar ratio. Even if this is not, in fact, due to a difference in penetration, the binding of copper or some other metal may yet be concerned with the spatial configuration of the sites favouring one acid rather than the other.

The growth-promoting activity of ethylenediamine tetraacetate has been variously reported as similar to that of indoleacetic acid[1,4], or as much less[5,6], according to the techniques and plant material used; with the strain of wheat used by Fawcett *et al.*[6], and using their technique, we have been able to reproduce their results. However, even if the growth-promoting activity of these two agents be accepted as of the same order of magnitude, the fact remains that their *in vitro* complexing activity differs vastly. It is, in fact, surprising that so powerful a chelating agent as ethylenediamine tetraacetic acid does not disrupt the chemical organization of the cell at many sites; the growth-promotion obtained may be the net result of stimulatory and inhibitory processes due to competition with various chelating agents in some such way as that suggested by Burström and Tullin[7].

Evidence seems to be accumulating that known natural and synthetic growth substances can form complexes *in vitro*[8,9], but more important than this is the question whether they do so in controlling growth in the living plant. Some of the evidence for this was very briefly reported in the communications cited[1,2] and the results of these and other experiments will be published in detail as soon as possible.

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

A New Ionospheric Phenomenon

In recent years, there have been reports[1–4] of sporadic radio-frequency radiation associated usually with auroral activity. However, it has always been difficult to establish an unambiguous identification because similar effects could be caused by man-made noise or interference. The special programme initiated at Jodrell Bank in October 1958 to study these unusual radiations provided a high degree of flexibility by using five separate total-power receivers, all on slightly different frequencies near 80 Mc./s., to monitor continuously various sectors of the sky. At present, two of the aerials are directed at 30° elevation above the northern horizon, one is directed at the zenith, one at 30° above the southern horizon and the other is rotated continuously so that Cassiopeia 23*N*5*A* is always in the beam. Three of the equipments are at Jodrell Bank and the others are on individual sites about 1 km. away. This experimental arrangement allows easy discrimination against localized interference at any one site, and against distant narrow-band radio signals.

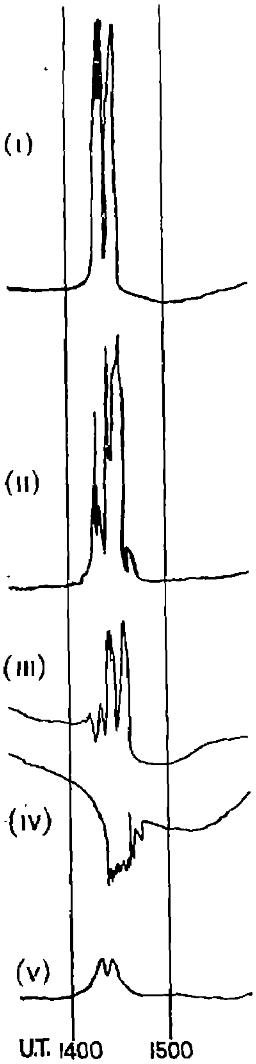

Fig. 1. Records from (I) northerly, (II) northerly (low sensitivity), (III) continuously following Cassiopeia, (IV) zenithal and (V) southerly aerials

Normal records from the equipments show the expected diurnal variation due to the galactic background and, in addition, the southern aerial records radio bursts and noise storms of solar origin. However, during the period January 3–10, 1959, there occurred about ten instances of isolated increases in the noise-level recorded by some of the instruments, together with *simultaneous decreases* in the others[5]. A further very striking isolated event occurred on March 25, 1959, at about 1400 U.T. The records are reproduced in Fig. 1. It can be seen that the northerly channels (i) and (ii) showed very strong enhancements in the signal level. The amplitude of (i) was greater than 150 per cent of the diurnal change in galactic level, and the increase in (ii) was 400 per cent of the diurnal galactic change. The former instrument was driven off-scale while the latter was operating at reduced sensitivity. The apparatus continuously following Cassiopeia (iii) with its aerial directed at this time toward the north-west showed a strong enhancement of approximately 50 per cent of the diurnal galactic range. The zenith instrument (iv) recorded a marked decrease of at least 50 per cent of the diurnal range of galactic intensity, while the south (v) indicated a weak increase of about 25 per cent. Since the back-to-front rejection ratio of the south-looking Yagi aerial is about 1 : 10, it is probable that the apparent southerly increase is spurious in view of the very strong northerly signal. At the time of this event the Sun was actually in the beam of the south aerial, hence one may conclude that direct solar radio-frequency radiation was negligible.

The Jodrell Bank magnetometer revealed a change in the horizontal component of the Earth's field coinciding with these observations. The change of about 50 gammas is the most significant fluctuation in an interval of 4–5 hr. However, the significance, if any, of the magnetic crochet is masked by the presence of other fluctuations of comparable size both earlier and later in the day.

This event, with its simultaneous radio-frequency emission and absorption in different sectors, is more intense than any observed in the January 1959 series. However, it has the same essential characteristics. The suggestion has been made[5] that this phenomenon is caused by passage through the ionosphere of streams of charged particles of very high velocity presumably of solar origin. In the upper ionosphere such particles stimulate the generation of radio-frequency energy while at lower levels the result is a net absorption of the background signal. The absorption mechanism is rather well established, especially in polar regions, and may be attributed to the production of abnormally dense ionization in the lower ionosphere. However, very little is known of processes which can generate radio-frequency noise in our atmosphere. It is believed that the impact of charged particles, both of high velocity and high density, is consistent with the environment for production of Čerenkov-type radiation. Other processes are also being considered.

Events of the type described seem to be rare. It is significant that both the first event of the group in January already reported, and the isolated event of March 25, seemed to be the precursors of a period of intense solar activity with associated terrestrial events such as magnetic storms and auroræ. A preliminary investigation has failed to reveal any unusual solar or other terrestrial effects which may be associated with this phenomenon.

We wish to acknowledge the continued interest and enthusiastic support of Prof. A. C. B. Lovell in this research.

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* Temporarily from the Carnegie Institution, Washington.

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Observations of Intense Ionization of Long Duration below 50 km. Altitude after some Strong Solar Flares

THE existance of ionized layers (the *C*-layers) in the lower and middle atmosphere (between 5 km. and 60 km. altitude) was suggested more than twenty years ago by several authors and such short-range echoes (20–50 km.) have also been reported in recent years. It seems doubtful, however, whether they were produced by ionization[1]. Landmark[2] has recently obtained a few echoes from a height of 65 km., which seem to have been of ionospheric origin. They appeared during periods of strong solar disturbances. Intense ionization at still lower heights was observed four times during the summer of 1958 at Kiruna Geophysical Observatory, Sweden.

The total non-deviative ionospheric absorption of 27·6 Mc./s. radio waves is being measured at the Observatory on a routine basis by means of a so-called 'riometer' (relative ionospheric opacity meter) designed by C. G. Little[3] at the Geophysical Institute, College, Alaska. The riometer is a self-balanced radio noise telescope using a vertical three-element Yagi antenna and having a so-called minimum detector, which makes measurements possible of the cosmic radio-noise level even in the presence of strong interference. The recorded cosmic-noise flux gives a relative measure of the overall absorption in the ionosphere.

On four occasions during the summer of 1958 very strong absorption was observed to start a few hours after the outbreak of solar flares of importance 3+. In three of these cases the maximum day-time absorption[4] exceeded 15 db. At the time of the first observation, July 7, 1958, it was midnight sun in Kiruna, but during the other three periods of observations, starting on August 16, 22 and 26 respectively, the shadow of the solid Earth reached from 62 km. on August 16 to 125 km. on August 26 above the Earth's surface at midnight.

The ratio of negative ion density to free electron number density is a function of the hour angle, as one of the processes determining the ratio is photodetachment of electrons from negative oxygen ions, and thus the absorption is smaller during the night than during the day. The electron affinity of the oxygen molecule is approximately 1 eV., which means that the photons of almost the whole solar emission spectrum have sufficient energy for the photodetachment reaction.

The riometer records for the nights of August 16–17, 22–23, 23–24 and 26–27 were all curves of the type shown in Fig. 1. During the evenings the absorption decreased to a minimal, and almost constant, night-time value, although the shadow of the solid Earth reached levels varying between 44 and 53 km. only (average of four values, 48·3 km.) above the surface of the Earth. Similarly, absorption started to increase again in the mornings when the shadow of the Earth had reached heights between 39 and 55 km. (average of three values, 48·3 km.). During the morning of August 24, a geomagnetic sudden commencement started before sunrise, and therefore no observations could be made.

In two of the seven cases the record is concave upwards (cf. Fig. 1) during the whole transition period between day-time and night-time conditions. In those cases the time of end and beginning respectively of the transition is estimated to be in error by only some ± 3 min. This corresponds to an uncertainty of height of less than ± 2 km. In the remaining five cases the uncertainty is about 5 km.

An explanation of the early arrival of the absorbing layer into the dark region may be that the effective shadow is not that of the solid Earth but of some layer in the atmosphere, for example, the ozonosphere. That explanation can, however, be ruled out by the following facts. It has been found at Stanford, California[5], that the intensity of reflexions on 325 kc./s. tends to increase when the solar rays tangential to the Earth strike the lower *E*-region, and the height of the lowest observed *E*-region reflexion on 100 kc./s. was found to drop appreciably at about the time when the region left the shadow of the solid Earth. These effects are attributed to electron photo-detachment, as in the cases under discussion here. Furthermore, the investigations of the distribution of ozone with height, using the eclipsed Moon as reflecting surface[6], are based on the fact that visible radiation, even in the Chappuis diffuse absorption bands of ozone, penetrates the Earth's atmosphere at the ozone-levels, reaches the eclipsed Moon and is reflected back to the spectrometer on the Earth's night-side. As all radiation of wave-lengths less than approximately 12,000 A. can produce free electrons by photo-detachment from O_2^- ions, the only remaining explanation of the fact that the illumination of the layers above the heights mentioned earlier does not result in any measurable radio-wave absorption in addition to that of the lower layers, seems to be that all but a negligible fraction of the ionization is situated below the heights in question. At such great depths in the atmosphere the absorption coefficient is in fact not increasing with depth as it is in higher levels, due to the fact that for very high values of the electron collision frequency the absorption decreases again. The transition-level is situated between 50 and 60 km.

If one takes into account the possible complete opacity of the lowest few kilometres of the atmosphere, the upper limits of the absorbing layers, given above, are not raised by more than the same small amount (a few kilometres).

The observations reported here support the hypothesis that the ionizing agent on the occasions under discussion was protons, emitted by the Sun during the solar flares (see ref. 4, Hultqvist, B.). The very low recombination coefficients found for this kind of ionization[7] may perhaps also be associated with the

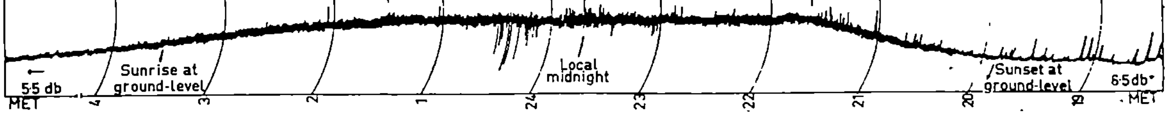

Fig. 1

fact that most of the ionization was situated within the ozonosphere, as is certainly the observed absence of magnetic effects of the ionization.

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Radio Reflexions from the Moon and Solar Corona

The ionospheric Faraday effect has recently been used[1,2] to determine the total electron content of the ionosphere. The rotation of the plane of polarization is assumed to be given by:

$$\varphi = 4{\cdot}72 \times 10^4 (f^{-2} B \cos\theta \sec\delta \int_{H_1}^{H_2} N \,\mathrm{d}h) \qquad (1)$$

where the limits of integration correspond to the ionospheric region in which the electron density is large enough to make an appreciable contribution to the rotation (for notation see ref. 2).

On the other hand, the theory of 'whistlers', investigations on the solar corona[3] and also the researches on the first Russian satellite[4] have led to the assumption that there are some hundred electrons per c.c. in the space around the Earth. This necessitates modification of formula (1). If we assume a constant electron density N_0 along the path from the outer ionosphere ($r = r_E + H_2$) to the Moon ($r = r_M$) we have:

$$\varphi = 4{\cdot}72 \times 10^4 f^{-2} \left\{ B \cos\theta \sec\delta \int_{H_1}^{H_2} N \,\mathrm{d}h + N_0 \int_{r_E + H_2}^{r_M} B \cos\theta \,\mathrm{d}r \right\} \qquad (2)$$

or, to a good approximation:

$$\varphi = 4{\cdot}72 \times 10^4 f^{-2} B \cos\theta \left\{ \sec\delta \int_{H_1}^{H_2} N \,\mathrm{d}h + \tfrac{1}{2} . N_0 (r_E + H_2) \right\} \qquad (3)$$

With $(r_E + H_2) = 7{\cdot}4 \times 10^8$ cm. and $N_0 = 10^3$ cm.$^{-3}$, we get $3{\cdot}7 \times 10^{11}$ cm.$^{-2}$ for the second term, while $\int_{H_1}^{H_2} N \,\mathrm{d}h$ is about 100×10^{11} cm.$^{-2}$. Hence we can estimate that in many cases the error introduced by neglecting this second term will not be important, and that, for example, the results obtained on the new F-layer model[5] will not be influenced strongly. But at times of small solar activity, the electron density in the ionosphere will decrease considerably and then we cannot neglect the electrons in the space around the Earth. In these and some other cases (for example, in the polar regions) we must take the revised formula (2) into consideration.

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Nature of Fluorescence of Uranium in Fused Sodium Fluoride

Although the property of fluorescence of uranium in sodium fluoride melts has been used to determine uranium quantitatively for the past 25 years, it is not known in what form the uranium exists in these melts. It has been the belief that the fluorescence in fused salts is due to a uranyl compound, but the evidence is not conclusive[1,2]. The intensity of fluorescence of the melts is so sensitive to slight variations in the fusion process that it is necessary to standardize all manipulations to obtain reproducibility. The cause of this sensitivity has not been explained. In an attempt to explain it several different uranium compounds were fused in different atmospheres. The intensities of fluorescence of the melts as well as fluorescence and absorption spectra were measured.

All the uranium compounds used for the experiments were made in this Laboratory. A sample of uranium tetrafluoride was also obtained from Harwell. A very high standard of purity is required as many impurities quench the uranium fluorescence. The sodium fluoride used was 'Baker analysed' and was specially prepared for use on the fluorimeter. This brand of flux was found to be entirely free of sodium carbonate, which is useful at times but not essential, as sodium fluoride–sodium carbonate flux mixtures are often used. Sodium fluoride decomposes during fusion to form small quantities of sodium carbonate when moisture and carbon dioxide are present in the atmosphere[3].

UO_3, U_3O_8, UO_2, UF_4 and $UO_2(NO_3)_2$ were fused with sodium fluoride in air at 1,160° C. and all melts fluoresced strongly. The high fluorescence of UF_4 was unexpected since uranium (IV) compounds have not been known to fluoresce. A test was devised to determine the valency of the uranium in the melt, using the property that cupferron precipitates uranium (IV) but not uranium (VI) in 10 per cent sulphuric acid solution.

Two separate portions of a solution containing uranium (IV) in 10 per cent sulphuric acid were treated with cupferron. Sodium fluoride had first been added to one portion, when a powdery green precipitate had formed. No further precipitation occurred on the addition of cupferron. The uranium (IV) in the second portion was immediately precipitated by cupferron. The sodium fluoride thus reacts with uranium (IV) probably forming a double fluoride, namely, $NaUF_5$ as reported by Katz and Rabinowitch[2]. This compound was found to be non-fluorescent.

This test was repeated using a melt in which uranium tetrafluoride had been fused in air with a low-melting mixture of sodium fluoride and sodium carbonate. When it was dissolved in 10 per cent sulphuric acid no green powdery precipitate settled out and the uranium was also not precipitated by cupferron. From this it was concluded that the uranium is oxidized to the hexavalent state during the fusion process.

The fluorescent species resulting from fused uranium tetrafluoride is therefore not tetravalent as the compounds examined by Zachariasen[2] appear to be.

The fusion of all the uranium compounds was repeated using an argon atmosphere in a tube furnace. All melts were fluorescent but intensities were much reduced. When oxygen was added to the atmosphere the intensities of the argon-fused melts increased in most cases. This seems to indicate that oxygen is required for high fluorescence. The initial fluorescence in argon, particularly of uranium tetrafluoride, appears to be due to the presence of minute quantities of oxygen which diffuse through the walls of the rubber tubing. This is very difficult to eliminate.

When sodium hydrogen fluoride is used as a flux in air with U_3O_8, UF_4 and $UO_2(NO_3)_2$, the usual high fluorescence is obtained, but when fusions are made in argon virtually no fluorescence occurs. This is ascribed to the action of hydrogen fluoride that is evolved from the flux on heating. Katz and Rabinowitch report that very small quantities of hydrogen fluoride are sufficient to prevent the oxidation of $UF_4.H_2O$ during dehydration at 400° C. Hydrogen fluoride also prevents the formation of oxy compounds[2].

The fluorescence spectra of the melts were examined and several variations were measured. The spectrum extended from approximately 5100 to 6500 A. Under certain conditions the lowest band limit ended at 5350 A. The main variations occurred in the violet region where bands appeared and disappeared according to the atmosphere, concentration, time of fusion and rate of cooling.

The spectra of uranyl salts do not vary in this manner. They consist of 6 or 7 bands extending from approximately 4600 to 6400 A. which shift nearer to or farther from the red region, depending on the composition of the salt.

The variation in the spectrum of the sodium fluoride – uranium melts appears to be the cause of the inconsistent intensities. It is not known what this variation is due to but it is suspected that an oxygenated uranium compound, with a variable constitution, is responsible.

The absorption spectra of argon-fused $UO_2(NO_3)_2$, UF_4 and U_3O_8 were measured on the Beckman *DU* spectrophotometer. Clear disks were obtained only when carbonate-free sodium fluoride was used. Melts fused in air became opaque due to the formation of sodium carbonate during fusion. These could not be measured on the spectrophotometer. The spectra of the pale yellow disks were measured against a blank of clear, colourless fused sodium fluoride.

In each spectrum maximum absorption occurred at 290 mμ. Absorption decreased steadily to 410 mμ and levelled off. No further peaks occurred, but each has a plateau from 350 to 360 mμ. Two of these curves are shown in Fig. 1.

Uranyl salts all have absorption peaks[4] in the region 400–500 mμ, while uranium (IV) absorbs in an entirely different manner[5]. The spectra of the fused melts resemble those of diuranates, which absorb strongly at 320 mμ with no further peaks occurring at higher wave-lengths[6].

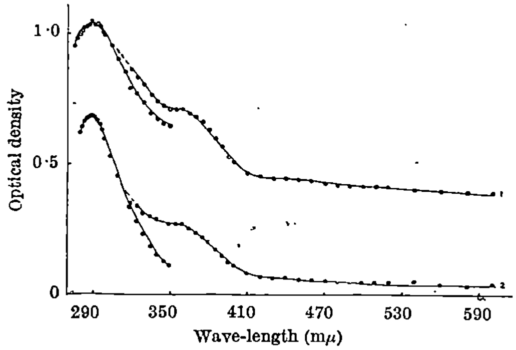

Fig. 1. Top, absorption spectrum of argon-fused uranyl nitrate using hydrogen and tungsten lamp sources; bottom, absorption spectrum of argon-fused uranium oxide (U_3O_8) using the same light sources

Uranyl salts are not stable at high temperatures. When ignited above 350° C. they decompose to form oxides. In the presence of a flux such as sodium fluoride which melts at 997° C. this decomposition must also occur, so that by the time the flux is molten the uranium is probably all present as U_3O_8. This then reacts with or dissolves in the molten sodium fluoride.

The fluorescent species formed does not resemble any of the parent compounds. It appears that any uranium compound can be fused with sodium fluoride at 1,200° C. to form the same or similar species provided that oxygen, moisture and several other constituents are present in the atmosphere. The best atmosphere for this is air.

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CHEMISTRY

An Automatically Operating, Coulometric Titration Method for continually measuring Small Amounts of Water in Fluids

SEVERAL batch-wise methods for the determination of small amounts of water are known. However, most of these methods lack general applicability.

In the method described here we have applied the well-known and versatile principle of the Karl Fischer titration. According to this titration procedure, the water to be determined reacts with the so-called Karl Fischer solution, a mixture of sulphur dioxide, iodine, pyridine and methanol. The simplified net reaction can be represented as:

$$SO_2 + I_2 + H_2O \rightarrow SO_3 + 2\,HI \qquad (1)$$

Pyridine and methanol act both as solvents and as complexing agents.

However, contrary to the classical procedure, iodine is generated and measured coulometrically[1]. It is generated by anodic oxidation of a modified Karl Fischer solution, in which the iodine is replaced by hydrogen iodide. At the anode, the following reaction occurs:

$$2\,I^- \rightarrow I_2 + 2e \qquad (2)$$

Automatic and continuous operation is realized as follows: a constant sample stream (for example, an alcohol with a water content less than 2 per cent and a rate of flow ranging from 10 to 100 ml./hr.) is supplied to the coulometric cell (see Fig. 1). In this cell, iodine is generated at the platinum wire electrode, *w.e.* The anode compartment is separated from the cathode compartment by a sloping, sintered glass disk to avoid redox cycles. The magnitude of the generating current i_g is controlled by a combination of an amperometric system and an electronic control system, so that sufficient and no excess iodine is generated for reacting with all of the water entering the cell. In this case the generating current—which can be recorded in simple manner—is a linear function of the water content of the sample. From Faraday's law, 1 μgm./sec. of water supplied to the cell needs a generating current of 10·72 m.amp., provided the current—as well as the titration—efficiency of the electrochemical reaction is 100 per cent. It appears that 100 per cent current efficiency is obtained when the current density does not exceed a critical value, dependent on the conditions of flow. The titration efficiency is—as in the classical titration—not 100 per cent; it is, however, constant, the actual value being dependent upon the composition of the electrolyte.

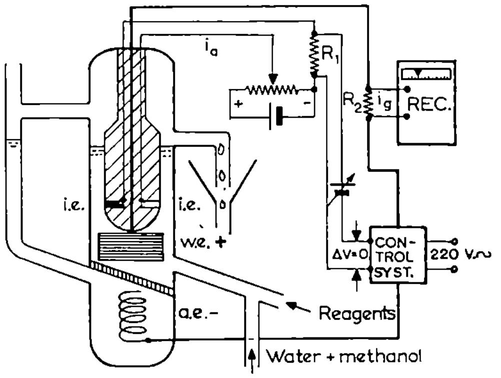

Fig. 1. Diagram of the hygrometer. *w.e.*, Working electrode (anode); *a.e.*, auxiliary electrode (cathode); *i.e.*, indicator electrode

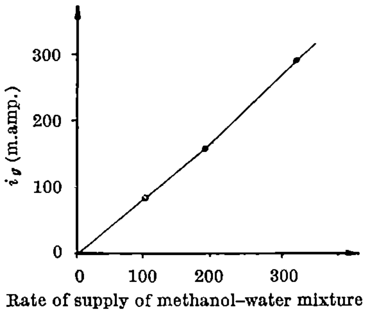

Fig. 2. Generating current i_g (in m.amp.) as a function of the rate of supply of a methanol–water mixture (in arbitrary units)

The amperometric system consists of two platinum electrodes, placed in an equipotential surface and provided with a potential difference of 25 mV. The generating current is so controlled that when the amperometric current i_a exceeds a fixed value of some microamperes (for example, when the water content of the sample decreases), the generating current decreases, etc. Environmental moisture must be excluded rigidly.

A laboratory apparatus built according to the above principles has worked satisfactorily. A typical graph is reproduced (Fig. 2) showing the generating current as a function of the rate of supply of a methanol–water mixture of a definite composition, the speed being expressed in an arbitrary measure.

While preparing this communication, our attention was directed to a recent paper by Meyer and Boyd[1], who have applied the same principle to the batch-wise titration of water.

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Molecular Symmetry in *Cyclo*pentadienyl Thallium and Some Related Substances from their Microwave Spectra

It was recently found in this laboratory[1] that the symmetry of *cyclo*pentadienyl nickel nitrosyl is simply and unequivocally shown by its microwave spectrum. We have now applied the same method to demonstrate the symmetries of *cyclo*pentadienyl thallium, *cyclo*pentadienyl manganese tricarbonyl and benzene chromium tricarbonyl. The manganese compound had sufficient vapour pressure at room temperature, but the other materials were studied in a Stark modulation spectrometer operated at about 100° C.

Several transitions of each substance were measured between 20 and 40 Gc./s. The spectra are those of strictly symmetrical-top molecules, with values of B, in Mc./s., as follows: *cyclo*pentadienyl thallium-205, 1465·10 ± 0·05; *cyclo*pentadienyl thallium-203, 1467·98 ± 0·05; *cyclo*pentadienyl manganese tricarbonyl, 826·5 ± 0·5; benzene chromium-52 tricarbonyl, 729·8 ± 0·5. Fine structures were not resolved, but spectra of molecules in excited vibrational states occurred, especially for the carbonyls. For these, B refers to the state showing the strongest absorption, but it is not certain that this is the ground-state. For *cyclo*pentadienyl thallium the lines are sharper, and those due to vibrationally excited molecules occur at lower frequencies than the ground-state absorptions. Separate series of lines due to *cyclo*pentadienyl thallium-205 and thallium-203 are recognized from their pattern and intensities.

The spectra prove that the *cyclo*pentadienyl compounds have axes of C_{5v} symmetry perpendicular to the C_5- and H_5-rings, and passing through the metal atoms. In benzene chromium tricarbonyl the corresponding axis is doubtless one of C_{6v} symmetry but, so far as microwave spectra can show, the symmetry might be merely C_{3v}. The tricarbonyl groups $(CO)_3$, when present, have C_{3v} symmetry about these same axes. The structure of *cyclo*pentadienyl thallium is thus the 'half-sandwich' type favoured by Cotton and Reynolds[2] on the basis of infra-red spectra. The tricarbonyls each have eight structure parameters, and detailed discussion is not profitable; but the values of B are consistent with dimensions expected from the study of related molecules. *Cyclo*pentadienyl thallium has only four structure parameters and, while a complete determination is not yet possible, it is profitable to examine carbon–carbon and carbon–thallium distances which are permitted for all reasonably likely values of the parameters affecting the hydrogen atoms. The simplest preliminary assumption is that the C_5H_5 system lies in one plane. With this assumption only, the distance from the thallium to the centre of the ring is found as 2·41 ± 0·01 A. If, in addition, we take d_{CH} as 1·08 A., we obtain $d_{CC} = 1{\cdot}43 \mp 0{\cdot}02$ A. and $d_{CTl} = 2{\cdot}705 \mp 0{\cdot}005$ A. The errors stated are those which could arise from possible inaccuracy in measurement of the small thallium isotopic shift; effects of changes in zero-point energy have been neglected. A variation in the value assumed for d_{CH} of $\pm$ 0·02 A. leads to additional changes of only $\mp$ 0·004 A. in d_{CC} and $\mp$ 0·002 A. in d_{CTl}. We have also investigated the effects of allowing the CH bonds to be bent out of the C_5-plane. An angular displacement of 5 deg. away from the thallium atom in these bonds leads to an increase of 0·025 A. in d_{CC}, and a decrease of 0·007 A. in the distance from the thallium to the centre of the ring. The distance d_{CTl} is increased by only 0·003 A. Its effect on d_{CC}, and general considerations, suggest that such bending is of small magnitude.

On such a basis, the C_5-ring appears to be similar in size to that found in ferrocene[3], with the possibility of being somewhat larger. The carbon–thallium distance is certainly longer than anticipated by Cotton and Reynolds[2], but there is very little evidence on which to base a prediction. From available data[4], a length of 2·4 A. would not seem impossible for a simple Tl–C linkage, and a greater length is naturally expected in a complex of this type. The distance found, however, coupled with the estimates of overlap integrals by Cotton and Reynolds[2], strengthens the evidence that ionic binding is important in this linkage. From microwave data for metallic halides as ion-pairs, Honig, Mandel, Stitch and Townes[5] tabulate ionic radii for such systems. From these and similar results for the largely ionic gaseous thallous halides[6], the corresponding radius for Tl^+ must be close to 1·0 A. The structure $C_5H_5^-\ Tl^+$ would thus require the $C_5H_5^-$ ion to have an axial radius of about 1·4 A., which does not seem unreasonable. While the structure can scarcely be entirely ionic, a considerable ionic character would not be out of keeping with the findings for the thallous halides.

A detailed report, with fuller discussion, will appear elsewhere. We thank Prof. G. Wilkinson and Dr. M. C. Whiting for gifts of materials, the Royal Society for the loan of equipment and Prof. J. C. Robb for his interest in this project. Two of us (J. K. T. and A. P. C.) acknowledge maintenance grants from the Department of Scientific and Industrial Research.

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Molecular Motion of Enclathrated Compounds as studied by Nuclear Magnetic Resonance

It has been known for some time that hydrogen-bonded crystals such as quinol and urea can enclathrate a variety of molecules. Many studies of the structures of clathrates by X-ray diffraction[1–4] and infra-red spectroscopic techniques[5] have yielded little information about the motions of the enclathrated molecules. In special cases, for example, oxygen and nitric oxide enclathrated in quinol, where the trapped molecule is paramagnetic, magnetic susceptibility measurements[6–8] have indicated that the trapped oxygen and nitric oxide molecules behave rather like free gas molecules.

For enclathrated molecules which are not paramagnetic it seemed that nuclear magnetic resonance spectroscopy would provide information about the motion of the trapped compound. We wish to report some preliminary results which we have obtained by studying the proton magnetic resonance signals from certain enclathrated hydrocarbons.

Though a wide range of clathrates are currently under investigation by a variety of methods, we shall give here only some results for magnetic resonance studies on urea hydrocarbon adducts, the hydrocarbon ranging from C_{7-13}, C_{16} and C_{26}. The urea/hydrocarbon adducts were prepared by the addition of the calculated amount of hydrocarbon to a saturated solution of urea in either methanol or in *iso*propanol. The solution was cooled slowly in a lagged Dewar vessel. The largest crystals (about 15 mm. long) were removed and dried. The proton magnetic resonance spectra were measured at 25° C. on a Varian 4300 *B* dual-purpose nuclear magnetic resonance spectrometer with a 12-in. magnet. The spectra were observed at a frequency of 40 Mc./s. and a magnetic field of 9,400 gauss.

All the adducts studied showed similar spectra. These showed a broad resonance line of 6·9–7·1 gauss half-width, mainly due to the protons of the urea cage, and a narrow line of about modulation width due to the protons of the enclathrated hydrocarbon molecules. By using minimum modulation (30 milligauss) and sweeping slowly through resonance (0·09 gauss/min.) the narrow resonance line observed for the urea/hexacosane adduct was estimated to be about 0·25 gauss wide. Fig. 1 shows a smoothed outline of a typical proton magnetic resonance spectrum observed for the hexacosane/urea adduct. Fig. 2 shows the proton magnetic resonance spectrum of hexacosane (m.p. 56° C.) itself under the same conditions. The main resonance peak is approximately 8·0 gauss wide, and the second peak is pre-

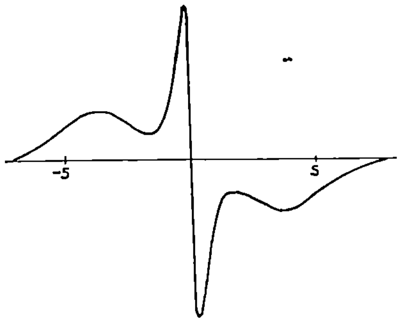

Fig. 1. Smoothed outline of derivative of typical proton magnetic resonance spectrum in *n*-hexacosane/urea adduct at 25° C.

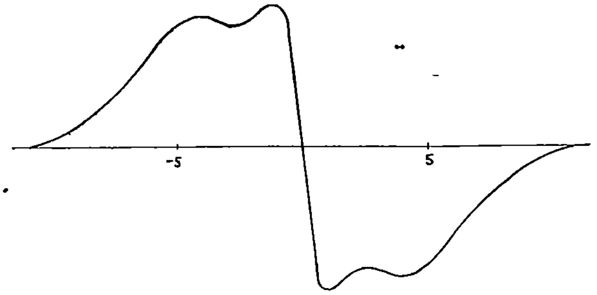

Fig. 2. Smoothed outline of derivative of typical proton magnetic resonance spectrum of n-hexacosane at 25° C.

sumably due to rotation of the terminal methyl groups.

To confirm that the narrow resonance line observed (Fig. 1) for the hydrocarbon/urea adduct was due to the protons of the enclathrated hydrocarbon we studied the proton magnetic resonance spectrum of the n-hexadecane/urea-d_4 adduct. Only a narrow line comparable with that shown in Fig. 1 was observed. This, of course, indicates that the enclathrated hydrocarbon molecules are rotating with some freedom, or executing torsional oscillations, about an axis parallel to the length of the channel in the urea complex.

In contrast to the results given above for urea/paraffin adducts we have observed that the thiourea/*cyclo*hexane clathrate spectrum at 25° C. has a line width of about 1·4 gauss due to the protons of the *cyclo*hexane molecule. *Cyclo*hexane[9,10] itself has, of course, a very narrow proton magnetic resonance absorption peak at 25° C. The broadening we observed when the *cyclo*hexane is enclathrated in thiourea is obviously due to the restriction of the motion of the *cyclo*hexane molecules in the thiourea cage. The crystal structure[4] of the thiourea/*cyclo*hexane clathrate is known. From this it is easy to see how the normal rotations of the *cyclo*hexane molecule at 25° C. are greatly restricted, or eliminated, when this molecule is enclathrated in thiourea.

We are continuing these researches and are determining the line-widths of the proton magnetic resonance signals over a wide range of temperatures. It is hoped that the results will provide useful information concerning the interaction between the matrix and the enclathrated molecules.

This work has been supported by grants from the National Research Council of Canada and we are most grateful to that body for its generosity.

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BIOCHEMISTRY

Milk as an Eluant of Polycyclic Aromatic Hydrocarbons added to Wax

PROTEINS in aqueous solution have been demonstrated to elute polycyclic aromatic hydrocarbons from soot particles. The liberated hydrocarbons, although hydrophobic, are retained in solution by the proteins[1]. We wished to determine whether milk, a protein solution, would elute incorporated polycyclic aromatic hydrocarbons from paraffin waxes despite the hydrophobic nature of the hydrocarbons.

Dairy waxes as used commercially to impregnate milk cartons were selected as the vehicle for incorporation of polycyclic aromatic hydrocarbons. It should be emphasized that the elution results reported here relate exclusively to the polycyclic aromatic hydrocarbons which were *added*, rather than to those occurring naturally in dairy wax. However, an analysis of several dairy waxes revealed the presence of a small amount of 1,2,5,6-dibenzanthracene of the order of one part per million in one of them. No 3,4-benzpyrene could be detected at levels as low as 1 in 10^9. The two polycyclic aromatic hydrocarbons chosen for elution studies were 3,4-benzpyrene and 1,2,5,6-dibenzanthracene. Both belong to the group of polycyclic aromatic hydrocarbons usually associated with petroleum derivatives, and their presence in unrefined paraffin waxes from which dairy wax is made is probable. Both these hydrocarbons are potent carcinogenic agents. Our interest in 3,4-benzpyrene is related to its ubiquitous environmental distribution; 1,2,5,6-dibenzanthracene is pertinent because of its demonstration in a particular wax used for coating milk cartons.

Table 1. ELUTION OF ADDED CARBON-14–3,4-BENZPYRENE FROM DAIRY WAX (54 HR.)

	Temperature	
	20° C.	5° C.
Whole milk	94 per cent	63 per cent
Half and half*	91 ,,	43 ,,
Buttermilk	81 ,,	48 ,,
Skim milk	74 ,,	43 ,,

* Equal amounts of milk and dairy cream.

Waxed surfaces containing added amounts of both polycyclic aromatic hydrocarbons were prepared in test-tubes so that a surface area of 26 sq. cm., sufficient to hold 10 ml. of milk, resulted. This represents between 3 and 4·6 times the ratio of waxed surface to milk content found in commercially available milk cartons. The thickness of the waxed layer lining the tubes varied from 75 to 250μ, while in milk cartons thicknesses were 75–100μ. The waxed layers were removed from the tubes by freezing in solid carbon dioxide with subsequent thawing. A stereomicroscope was used for measurement. As anticipated, elution from thin layers regularly occurred more rapidly than from thicker layers.

Four types of milk were selected for study: homogenized milk, skim milk, buttermilk, and a milk-cream mixture obtained commercially as 'half and half'. Differences in fat content and pH in the four milks chosen were expected to yield clues relative to the mechanisms of elution.

Room temperature and usual refrigerator temperature (5° C.) were selected for comparative studies as these are the two commonly encountered in milk

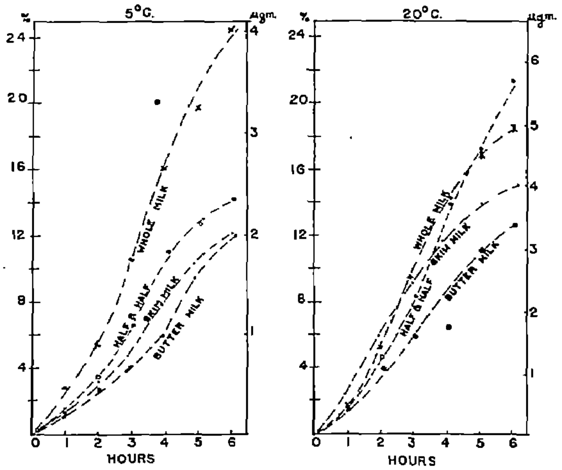

Fig. 1. Elution by milk of 3,4-benzpyrene added to wax

use. In numerous experiments we established that the elution at the two contrasting temperatures of 20° C. (room temperature) and 5° C. (refrigerator temperature) for the various milks was consistent and compatible. We therefore abandoned attempts at attaining identical thickness of wax and concentration of carcinogen when consonant results had been obtained.

The quantity of benzpyrene eluted by milk was determined at hourly intervals for the first 6 hr. of exposure by the difference in intensity of fluorescence between the maximum at 405 mµ and the minimum at 427 mµ. The increase in fluorescence intensity is given in Fig. 1 for each of the milks at room temperature and at 5° C. As we wished to obtain additional information on the completion of elution, the exposure of wax to the particular milks was continued for 24 hr. After the 24-hr. exposure, individual waxes were exposed to fresh samples of each type of milk for an additional 30 hr. At this time, fluorescence could be demonstrated primarily in the upper rim of wax which had not been in contact with the milk. At one extreme, for example, the total amount of benzpyrene retained in the wax after 54-hr. contact with a butter-milk sample was found to be 1·8 per cent. Carbon-14–1,2,5,6-dibenzanthracene was used rather than the unlabelled pure crystalline compound, as the minute amounts of the hydrocarbon used did not possess enough fluorescence energy to be detected.

Elution of benzpyrene and dibenzanthracene was observed in all milk samples studied. Homogenized milk was the best eluant, with the remaining three showing slightly less potency. There was almost total elution of polycyclic aromatic hydrocarbons during a 54-hr. period. The decrease in rate of elution incidental to the depletion of the waxes occurred as expected. At room temperature, the elution was more complete for all four types of samples.

The presence of the polycyclic aromatic hydrocarbons in milk cannot be attributed to a possible solubilization of the wax in milk. This was established by the addition of a strongly fluorescent wax to milk in all experimental circumstances and the subsequent failure to demonstrate fluorescence in the milk.

Milk, independent of its fat content, is an efficient eluting agent and solvent of benzpyrene and 1,2,5,6-dibenzanthracene from hydrophobic wax following the incorporation of these carcinogenic hydrocarbons into wax. This occurs in a manner that is compatible with both the temperatures usually encountered and the duration of contact of milk with the waxed carton.

This investigation has been supported by Grant *CS*–9156 from the Field Investigations and Demonstrations Branch of the National Cancer Institute and Grant *LC*–3 from the American Cancer Society.

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Detection of Hydroxyl Groups in Porphyrins and Chlorins

THE behaviour of porphyrin *a* [1] and chlorin a_2 [2], the iron-free prosthetic groups of cytochrome *a* and a_3 and cytochrome a_2 respectively, when run as the methyl esters on paper chromatograms in various solvent systems, suggests that these compounds contain a strongly polar group in one of the side-chains. In the case of porphyrin *a*, the formyl group, which is known to be present, would not alone account for the R_F values obtained.

To test the possibility that the polar characteristics of these two tetrapyrroles were due to the presence of a hydroxyl group in the molecule, the following technique was devised. The porphyrin, or chlorin, was acetylated in a mixture of acetic anhydride and pyridine (1 : 10 v/v) at room temperature overnight, the mixture was then poured into ether and the ether washed well with 0·1 per cent hydrochloric acid followed by distilled water. Paper chromato-

Table 1. R_F VALUES OF HYDROXYLATED PORPHYRINS AND CHLORINS, AND THEIR ACETYLATED PRODUCTS

Compound (methyl esters)	Chloroform–kerosene		Propanol–kerosene	
	Alcohol	Acetate	Alcohol	Acetate
1. Monohydroxyethyl deuteroporphyrin	0·34	0·64	0·38	0·68
2. Monovinyl-mono-hydroxyethyl deuteroporphyrin	0·29	0·60	0·34	0·66
3. Hæmatoporphyrin	0·03	0·56	0·18	0 57
4. Monohydroxymethyl deuteroporphyrin	0·19	0·54	0·24	0·57
5. Monohydroxymethyl monovinyl deuteroporphyrin	0·22	0·54	0·31	0·56
6. Dihydroxymethyl deuteroporphyrin	0·01	0·56	0·14	0·56
7. 2-Formyl-4-hydroxyethyl deuteroporphyrin	0·16	0·58	0·26	0·64
8. Porphyrin *a*	0·10	0·56	0·26	0·62
9. Dioxyprotoporphyrin*	0·15	0·56	0·30	0·58
10. 2-Ethyleneglycol deuteroporphyrin	0·30	0·64	0·32	0·61
11. 2-α-Hydroxymeso-rhodochlorin	0·31	0·80	0·34	0·78
12. 2-α-Hydroxymeso-chlorin p_6	0·33	0·82	0·35	0·80
13. 2-α-Hydroxymeso-phaephorbide *a*	0·10	0·78	0·34	0·72
14. Chlorin a_2	0·30	0·65	0·40	0·60

Compounds 3, 7, 8, 9, 13 and 14 were prepared according to known methods, compounds 1, 2, 4, 5, 6, 10, 11 and 12 by methods which will be published elsewhere in detail.

* *This compound contains only one hydroxyl group and one acetyl* side-chain (to be published elsewhere).

graphy of the acetates was then carried out in the chloroform–kerosene, or the propanol–kerosene systems of Chu *et al.*[3], and the R_F values obtained compared with those of the parent compound. These R_F values and those of a number of model hydroxylated porphyrins and chlorins and their acetates are given in Table 1.

The difference between the R_F value of a compound with a free hydroxyl group and that of its acetate is of some value in distinguishing between the presence of one or more hydroxylated side-chains in the molecule.

From the values given in Table 1 it is clear that porphyrin *a*, chlorin a_2, and dioxyprotoporphyrin[4], an irradiation product of protoporphyrin, each contain a hydroxylated side-chain, probably only one in each compound.

Further work is being carried out in this laboratory to determine the nature and position of the hydroxyl groups in these tetrapyrroles.

I wish to thank Dr. R. Lemberg for his interest and advice. This work was supported by a grant from the National Health and Medical Research Council of Australia.

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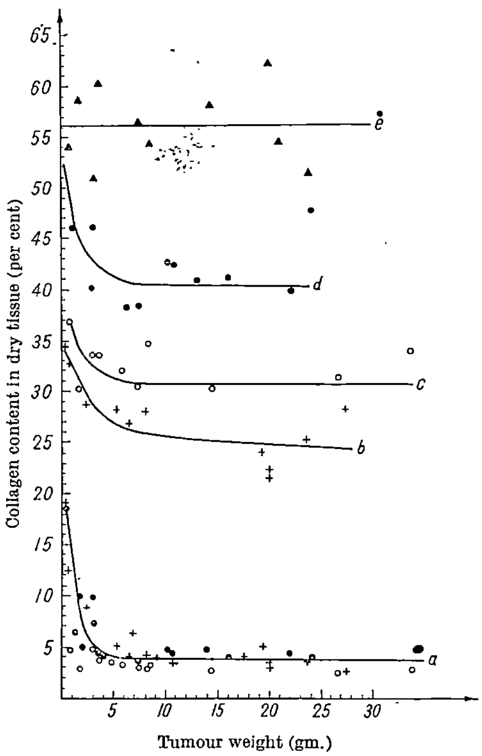

Fig. 1. *a*, Collagen content in rat neoplastic tissue during development of Guérin carcinoma in males (○) and during growth of sarcoma in males (●) and females (+). *b*, *c*, *d*, Collagen level in the tissue surrounding tumours under investigation. *e*, Arithmetic mean of collagen determinations in normal subcutaneous tissue of male tumour hosts (▲)

Collagen Content of Normal Connective Tissue, of Tissue surrounding a Tumour and of growing Rat Sarcoma

There have been several studies of the qualitative and quantitative changes produced in different components of connective tissue after treatment of normal animals with carcinogens[1]. However, little attention has been paid to the changes in the connective tissue during the growth of a tumour. This communication reports studies in the collagen content of neoplastic tissue, as well as of the tissue surrounding the tumour, during the development of the neoplasm in rats. The quantities of collagen in subcutaneous tissue taken from the upper part of the abdomen (at a considerable distance from the tumour) were taken as controls.

The experiment was carried out on male and female white rats aged 2–4 months. A fragment of Guérin carcinoma was implanted subcutaneously into the backs of 11 male rats, which formed one group of animals, and a fragment of transplantable sarcoma (42nd passage) first induced by methyl cholanthrene was implanted into the second group of 30 rats comprising both males and females. At different intervals between 3 and 30 days after grafting the tumour the animals were killed, and specimens of the tissues mentioned above were taken for determination of collagen by the Neuman–Logan method[2]. The method was modified by shaking the sample with the same volume of ethyl acetate just before reading the absorption. In this way the coloured impurities originating in either the reagent or the extract were removed. Fig. 1 shows the collagen content of the tissues investigated. Every point represents the mean of three parallel analyses.

Curve *a* shows the dependence of collagen content in the neoplastic tissue on weight of tumour. In the first stage of development of the tumour there is a rapid decrease in the collagen content, after which its level remains unchanged. The levels of collagen in neoplastic tissue of male and female rats bearing sarcoma as well as of males bearing Guérin carcinoma are of the same order. There are no significant differences in the collagen content depending either on the sex of the host or on the kind of tumour.

Curves *b*, *c* and *d* represent determinations of collagen in tissue surrounding the tumour. In contrast to the neoplastic tissue, here the level of collagen depends significantly on the sex of the host. The collagen contents in males bearing sarcoma are almost twice as high as in females bearing the same tumour. Moreover, in males the tissue surrounding the carcinoma contains less collagen than that surrounding the sarcoma.

The line *e* at the top of Fig. 1 represents the arithmetic mean of the collagen determinations; it characterizes the quantity of collagen in the normal subcutaneous tissue of male tumour hosts. It is evident that the collagen-level in normal tissue is higher than that in the tissue surrounding the tumour. This suggests that the subcutaneous tissue reacts to the tumour either by decreased synthesis or by increased catabolism of collagen.

The significant difference in the level of collagen in tissue surrounding the tumour in male and female rats bearing the sarcoma probably is the result of hormonal differences. The findings described above are in agreement with observations on the inhibition of collagen fibril formation caused by the œstrogens[3] and on the decreased collagen synthesis in female rats as compared with males[4].

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Glutamic–Aspartic Transaminase of Pig Heart Muscle

THE glutamic–aspartic transaminase of pig heart muscle has been more than 98 per cent resolved into apoenzyme and co-factor by carrying out a differential heat inactivation in phosphate buffer in the course of purification of the enzyme. The apoenzyme has been purified 64-fold, by relatively simple and reproducible techniques. The highest purification factor previously reported[1] for the apoenzyme is 26. The specific activity of the purified apoenzyme compares favourably with that of an electrophoretically homogeneous preparation of the holoenzyme[2]. Cammarata and Cohen's suggestion[3] that purification of the apoenzyme necessarily results in partial inactivation has been disproved, since it is possible to account for all the enzyme activity among the various protein fractions obtained at each step in the purification.

The initial rate of reaction between aspartate and α-ketoglutarate is linearly dependent on the concentration of the purified transaminase only up to 0·004 mgm. protein c.c.$^{-1}$. Above this level the dependence of reaction-rate on enzyme concentration deviates markedly from a linear relation. For the reverse reaction, the dependence of the reaction-rate on enzyme concentration is linear up to 0·01 mgm. protein c.c.$^{-1}$. This phenomenon has been reported for crude enzyme preparations[3,4]; but its consequences have not been considered in any kinetic studies reported hitherto. The following evidence does not support the suggestion[4] that the non-linear dependence of reaction-rate on enzyme concentration is due to the existence in solution of an equilibrium between active and inactive forms of the enzyme. First, the initial rate of reaction is unaffected by reagents known to break down protein aggregates, for example, benzene, ionic detergents and high salt concentrations. Second, when the same low concentration of pyridoxal-5′-phosphate (4γ c.c.$^{-1}$) is used for reactivation of a concentrated and dilute solution of the apoenzyme, equivalent amounts of enzyme taken from the two preincubation mixtures give the same initial rate of transamination on addition to the substrates. This shows that if aggregates are formed at high protein concentrations the aggregation is such that the sites occupied by the co-factor are not masked. Third, the proposed equilibrium between active and inactive forms of the enzyme must be established very rapidly since the observed initial rates of reaction depend only on the enzyme concentration in the reaction mixture and not on the concentration of the enzyme during the period of preincubation with the co-factor.

The variation of the rate of reaction with enzyme concentration is independent of the purity of the enzyme and is unaffected by the addition of a boiled extract of pig heart muscle. It is therefore unlikely that the non-linear dependence of reaction-rate on enzyme concentration is due to the presence of an inhibitor in the original protein extract.

Bonavita and Scardi[5] concluded that the co-factor was attached to the enzyme through the 4-formyl group and that this group was not free to take part in Schiff's base formation with the substrates as suggested by Snell and co-workers[6]. This conclusion was based on the absence of inhibition of transamination by cyanide ions when added, in excess, to the reactivated enzyme followed by 12 hr. dialysis before assay, whereas inhibition did occur when the cyanide ions were preincubated with the co-factor before reactivation of the apoenzyme. In the present work, using cyanide ions and pyridoxal-5′-phosphate in equimolar concentrations, the same degree of inhibition (75 per cent) was observed both when the cyanide ions were added to the reactivated enzyme and when the co factor was incubated with cyanide prior to reactivation of the apoenzyme.

The equilibrium constants for the reaction between the apoenzyme and the two forms of the co-factor have been measured under conditions in which there can be no shift in the equilibrium during the assay of the holoenzyme concentration. Previous determinations of the equilibrium constants[1,7] have been unsatisfactory because such precautions have not been taken. It appears that the true equilibrium constant for pyridoxal-5′-phosphate is some ten times greater than that for pyridoxamine-5′-phosphate.

Braunstein[8] has suggested that the equilibrium constant for the overall transamination reaction depends on the purity of the transaminase preparation used. The equilibrium constant has been determined using a highly purified enzyme solution, and the mean value of K, from some twenty determinations, is 6·50, in close agreement with the value of 6·74 found by Krebs[9] using a crude extract of horse heart muscle.

We wish to thank Prof. R. S. Nyholm for the interest he has shown in this work. The Nuffield Foundation is thanked for a grant for apparatus and for the award of a fellowship to one of us (K. G. O.). One of the authors (B. E. C. B.) acknowledges, with thanks, a research scholarship awarded by the Medical Research Council.

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Deoxyribonucleic Acid Content of the Cell-Nuclei in the Adrenal Medulla after Exposure to Low Temperatures

As has been shown by H. Roels[1] in other endocrine glands, I have found that, in the adrenal medulla of the white rat, there is a correlation between the mean deoxyribonucleic acid content of the nuclei and cell activity. A preliminary communication on this topic[2] reports an increase of the nuclear deoxyribonucleic acid content after stimulation by means of daily injections of insulin, and also an important decrease in the resting gland after bilateral splanchnectomy.

The present communication is devoted to experiments on stimulation of the adrenal medulla by means of exposure to low temperature ; the stress produces hypersecretion of adrenaline.

Five male rats were kept for a fortnight in a refrigerator at nearly 4° C. They were killed, together with five controls. The adrenals and a control testis were simultaneously fixed in alcohol, formol and acetic acid (75 : 20 : 5), dehydrated and embedded. Sections (10μ) of the different objects were mounted on the same slide, in order to obtain homogeneous Feulgen staining. The deoxyribonucleic acid content of the individual nuclei was measured *in situ* by Lison's histophotometrical method[3]. As the deoxyribonucleic acid contents obtained were given in arbitrary units, we used as a standard a 'theoretical diploid value', being half the mean content of 50 spermatocytes I measured in the control testis. The results are summarized in Table 1.

Table 1

	$\bar{x}$	$\log \bar{x}$	s	$s \log \bar{x}$	n
Spermatocytes I	2,663	3·425	0·004	0·006	50
	Theoretical $2s$ value, 1,332				
Controls 284	1,308	3·116	0·046	0·006	50
285	1,366	3·135	0·067	0·009	50
286	1,200	3·079	0·045	0·006	50
287	1,210	3·082	0·055	0·007	50
288	1,267	3·102	0·053	0·007	50
Pool	1,268	3·103	0·052	0·003	250
Cold-treated 289	1,469	3·167	0·043	0·006	50
290	1,426	3·154	0·039	0·005	50
291	1,389	3·142	0·042	0·005	50
292	1,372	3·136	0·034	0·004	50
293	1,446	3·160	0·039	0·005	50
Pool	1,414	3·150	0·041	0·008	250

As the different individual deoxyribonucleic acid contents of the nuclei present a log-normal distribution, the statistical computations are made using the logarithms of these values.

Comparing cold-treated animals and controls, it is clear that the stimulation of the adrenal medulla is accompanied by an increase in the mean deoxyribonucleic acid content of the nuclei, which for the pooled results reaches 11·4 per cent ($t = 7{\cdot}0$; $P < 0{\cdot}001$).

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New Types of Salting-out Paper Chromatograms of Antibiotics

ACCORDING to Miyazaki, Omachi and Kamata[1], antibiotics can be grouped according to their salting-out chromatograms. Pure antibiotics and materials containing antibiotics were examined by the aid of ascending paper chromatography. As irrigation solvents in each case and with each antibiotic, distilled water and rising concentrations of ammonium chloride (0·5, 1, 2, 3, 5, 10, 20 per cent and saturated) were used. Location of the spots of the antibiotics, that is, the R_F values, were ascertained bio-autographically.

Antibiotics were divided into four groups. In those of group *A* the R_F value is not correlated with the concentration of the ammonium chloride solution, identical values being found at all concentrations and in distilled water. To this group belong penicillin, grisein, chloramphenicol, aureothricin, and the special substance 2. In group *B* are those antibiotics which have an R_F value 0 in distilled water, and increasing R_F values with increasing concentrations of ammonium chloride. They are : streptomycin, streptothrycin, luteomycin, fuscomycin, xanthomycin and flaveolin. Group *C* is different from group *B*, displaying the highest R_F value in distilled water, and lowering of the values with increasing concentration of the solution of ammonium chloride. Members of this group are : actinomycin and griseoflavin. Group *D* consists of antibiotics which do not display any movement whatever in an irrigating solvent from the starting point ; eventually increased tailing tendency was observed with higher concentrations of the solutions of ammonium chloride. Aureomycin and terramycin are members of this group.

These results obtained by Miyazaki *et al.* have been confirmed by my experiments with salting-out paper chromatography of antibiotics. Moreover, I have been able to show the existence of other types of salting-out paper chromatograms of antibiotics with antibacterial action, of actinomycetal origin.

In group *E* are antibiotics which have an R_F value 0 in distilled water, and an initial increase with rising concentrations of the solution of ammonium chloride, the maximum being (R_F = nearly 1) in 5 per cent ammonium chloride. Thereafter a decrease occurs, as shown in Fig. 1. The line connecting the different R_F values is of the shape of a truncated parabola. This type of paper chromatogram was

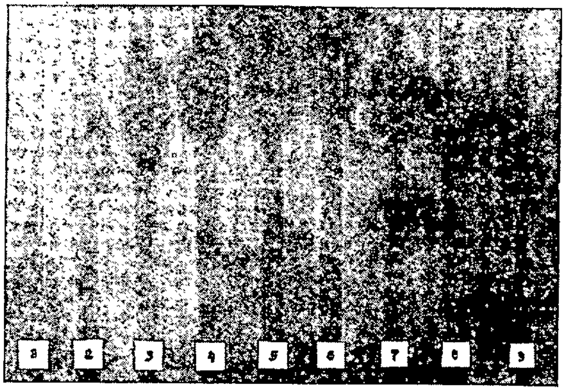

Fig. 1. The salting-out paper chromatogram of erythromycin. 1, Distilled water ; 2, 0·5 ; 3, 1 ; 4, 2 ; 5, 3 ; 6, 5 ; 7, 10 ; 8, 20 per cent ; and 9, saturated ammonium chloride solutions

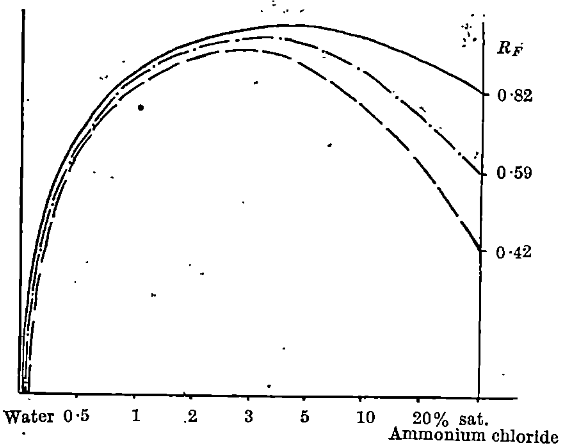

Fig. 2. Curves of the salting-out paper chromatograms of three macrolides. ———, Oleandomycin; –·–·–·, erythromycin; – – – – – –, carbomycin

found in the well-known macrolides (for example, oleandomycin, erythromycin and carbomycin). Within the group, further differentiation of these three macrolides was possible. The curvature of the truncated parabola—best demonstrated by the R_F value in saturated solution of ammonium chloride—is different in these three compounds. The slightest curvature occurred with oleandomycin, the R_F value in saturated ammonium chloride being 0·82; the maximal one with carbomycin (under identical conditions the R_F was 0·42). A midway position is occupied by erythromycin (R_F value being 0·59), as shown in Fig. 2. Obviously, the curvature of the truncated parabola is proportional to the molecular weight of these three macrolides. With the least curvature for oleandomycin is associated the least molecular weight (689); with the greatest curvature of carbomycin the highest one (844). As regards molecular weights, erythromycin is again midway between these (733).

At present, only one antibiotic can be placed in group *F*. This is desertomycin, produced recently by Úri *et al.*[2]. The characteristic feature of the salting-out paper chromatogram is the 0 value of R_F in distilled water. A rise of the R_F values is associated with increasing concentration of ammonium chloride up to 3–5 per cent; thereafter, however, R_F values decrease, and the value $R_F = 0$ is associated with saturated ammonium chloride solution. This type of chromatogram is shown in Fig. 3. By connecting the single R_F values, a paraboloid curve is obtained. This seems to unite groups *B* and *C* of Miyazaki *et al.*, the main representatives being streptomycin with primarily antibacterial activity, and actinomycin which is endowed with a cytostatic effect also. Desertomycin exerts an antibacterial as well as a cytostatic activity, as I have shown. Since this type of salting-out paper chromatogram has not been reported among antibiotics hitherto studied, in addition to its other characteristics, this feature is further proof that desertomycin is a new antibiotic.

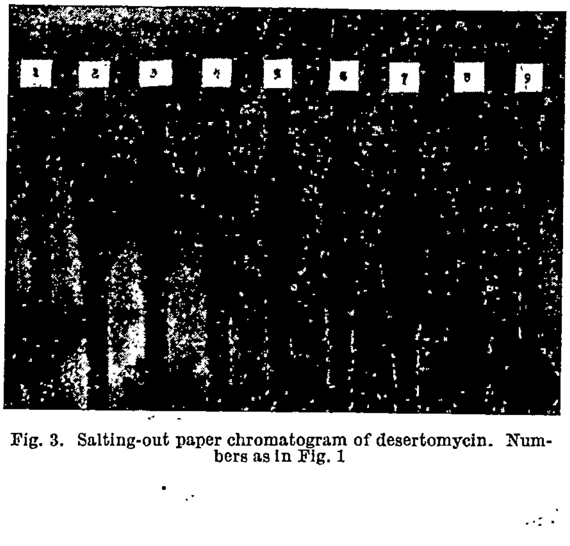

Fig. 3. Salting-out paper chromatogram of desertomycin. Numbers as in Fig. 1

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ANIMAL PHYSIOLOGY

Thyroxine-releasing Effect of Salicylate and of 2,4-Dinitrophenol

THE fact that salicylate increases the oxygen consumption in man was first observed by Denis and Means[1] in 1916. This observation has since been corroborated by several other investigators[2]. The oxygen consumption of tissues removed from animals treated with salicylate is likewise increased[3].

Coincident with the increase in metabolic rate, there is a decrease in the protein-bound iodine of the serum, and the fractional rate of disappearance of injected radiothyroxine from the circulation increases[2]. Furthermore, salicylate causes a reduction in the uptake of radioiodine by the thyroid[2], but the uptake is increased after stimulation by thyrotropin[4]. Similarly, 2,4-dinitrophenol can induce a rise in basal metabolic rate and a coincident fall in protein-bound iodine in the serum[5]. In experiments with laboratory animals, it has been found that dinitrophenol may reduce the uptake of iodine-131 by the thyroid[6]. The mechanisms by which salicylate and dinitrophenol act have not been elucidated.

All these observations could, however, be explained by an increase in the plasma level of free thyroxine, that is, thyroxine not bound to protein. It is presumably the concentration of free thyroxine which controls the quantitative biological effect of the thyroid hormone[7].

Austen, Rubini, Meroney and Wolff[2] found no change in the concentration of thyroxine-binding protein after salicylate administration. They concluded that the effects of salicylate could not be due to a change in the binding of thyroxine.

I have recently described a method for direct determination of free plasma thyroxine[8] which has permitted a renewed investigation of this problem.

The interaction between thyroxine (*Tx*) and thyroxine-binding protein (*P*) may be expressed by the reaction scheme:

$$Tx + P \rightleftarrows TxP$$

where the equilibrium is displaced so far to the right that less than one-thousandth of the total thyroxine is free.

Application of the law of mass action gives:

$$[Tx_f] = k\frac{[PBI]}{[P_{\text{unsat.}}]} \tag{1}$$

where Tx_f denotes free thyroxine and $P_{\text{unsat.}}$ unsaturated thyroxine-binding protein. On the assumption that all organic iodine present is in the form of thyroxine, TxP has been replaced by PBI in the equation.

It should thus be possible to obtain an estimate of $[Tx_f]$ if the unsaturated protein could be determined in addition to the protein-bound iodine, which may be analysed chemically.

If a tracer dose of radiothyroxine ($Tx^{131}I$) is added to a sample of serum, the following relationship will be valid after equilibrium has been established:

$$\frac{[Tx^{131}I_f]}{[Tx_f]} = \frac{[PB^{131}I]}{[PBI]} \tag{2}$$

When the expression (1) for $[Tx_f]$ is inserted in this equation, we obtain:

$$\frac{[Tx^{131}I_f]}{[PB^{131}I]} = \frac{K}{[P_{\text{unsat.}}]}$$

Thus it is seen that the denominator of the fraction in equation 1 can be calculated by determining the fraction of the added quantity of radiothyroxine that is present in the free state. ($[Tx_f]$ can also be calculated directly from equation 2.)

The determination was carried out as follows. A 'Plexiglas' vessel consisting of two separate, identical parts was assembled with a 'Cellophane' membrane between the two halves. In one of the chambers thus formed was placed 10 ml. of serum, to which radiothyroxine was added (chamber *A*). In the other chamber was placed 10 ml. of serum to which the same quantity of normal thyroxine was added (chamber *B*). The assembly was incubated in a constant-temperature bath with adequate stirring of the solution containing the radiothyroxine.

The free $Tx^{131}I$ passes through the membrane at a rate proportional to its concentration. During the first 24 hr., two samples of 4 ml. or three of 3 ml. were withdrawn from chamber *B*. At the same time an equal volume was removed from chamber *A*.

Since the $Tx^{131}I$ employed contained some inorganic iodine-131, the samples had to be washed carefully[9], after which the content of $Tx^{131}I$ was determined in a well-type scintillation counter. The result is expressed as per cent of the total $PB^{131}I$ in chamber *A*. Details of the experimental procedure are described elsewhere[8].

The results are shown in Fig. 1 and in Table 1.

Table 1. Effect of Addition of 2,4-Dinitrophenol

2,4-Dinitrophenol added (mgm./100 ml.)	Percentage increase of free thyroxine
0·5	9
1·0	18
3·0	25
5·0	38

As can be seen from Fig. 1 the salicylate evidently causes a substantial increase in the amount of $Tx^{131}I$ passing through the membrane. According to the above considerations this must be due to an increase in free thyroxine.

The thyroxine-releasing effect of salicylate and of dinitrophenol is probably a result of binding of these substances to some of the thyroxine-binding sites of the plasma proteins. Whether this is true only of the albumin or whether it also applies to the specific thyroxine-binding protein cannot be decided on the basis of the present investigations.

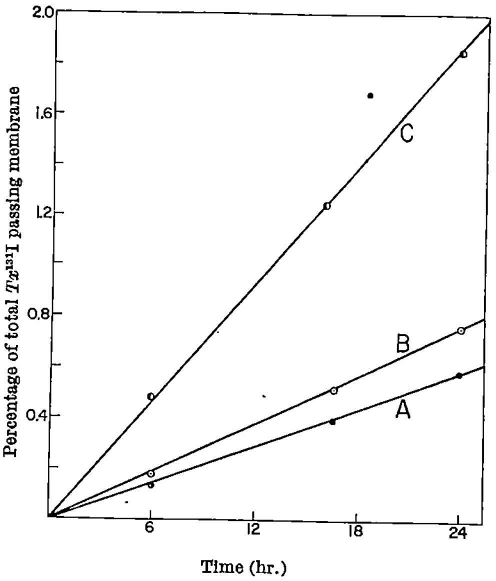

Fig. 1. *A*, Amount of $Tx^{131}I$ passing through the membrane at various times; *B*, effect of 10 mgm. sodium salicylate per 100 ml. added to both chambers; *C*, as *B* with 50 mgm. sodium salicylate

After administration of an ordinary dose of salicylate, the level in the plasma is in the range[2] 20–50 mgm./100 ml. Thus the above experiments can explain the rapid calorigenic action of salicylate, and also the fact that the action is transient. The increase in free thyroxine explains the increased fractional rate of disappearance of injected radiothyroxine and the fall in *PBI*. Furthermore, the fall in the uptake of radio-iodine by the thyroid, and the increase after administration of thyrotropic hormone, may be explained by the increase in free thyroxine.

Thus, the experiments definitely support the idea that it is the free plasma thyroxine that regulates the pituitary effect on the thyroid.

The dose of dinitrophenol that causes a calorigenic effect in man is 200–300 mgm./24 hr. period. This dose may well give rise to plasma concentrations of dinitrophenol within the concentration-range in Table 1. Possibly dinitrophenol also has a direct effect on the uncoupling of oxidative phosphorylation[10]. The effect may even be a more important factor in its calorigenic effect. However, the fall in protein-bound iodine and the possible fall in the thyroid uptake of radioiodine can presumably only be explained by the increase in free thyroxine.

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Influence of Dietary Cod-liver Oil and Some Fractions of Cod-liver Oil on Serum Cholesterol-level of Rats

FROM numerous experiments with humans and experimental animals it is known that the cholesterol content of the blood is greatly influenced by the amount and kind of dietary fat. In general, the relatively unsaturated vegetable fats decrease the serum cholesterol-level, while an increasing influence is observed with the relatively saturated animal fats. The highly unsaturated oils from marine animals, however, exert a potent cholesterol-lowering activity. This effect was observed in humans following the consumption of seal oil[1], sardine oil[2], whale oil[3] and pilchard oil[1,4] and also in rats fed sardine oil[5].

So far it is not yet decided what compounds of the fats are responsible for the action on cholesterol. The polyenoic acids, linoleic acid and arachidonic acid, applied in pure form, were found to be very active in lowering serum cholesterol-levels[6], whereas hydrogenation of highly unsaturated fats was accompanied by a decrease in activity[3,7]. These findings suggest that the fatty acid fraction is responsible for the effect observed. However, other experiments suggest that the unsaponifiable fraction of vegetable oils possesses cholesterol-lowering properties[8,9].

We have studied the cholesterolemic properties of cod-liver oil and some fractions thereof by feeding them to groups of 10–12 newly weaned rats in a hypercholesterolemic basal diet of the following percentage composition: casein 15, potato starch 10, wheat starch 57·5, minerals 4, vitamin mixture 2·1, choline chloride 0·2, hydrogenated coconut oil 10, cholesterol 1·0 and cholic acid 0·2. Different fats or fractions of cod-liver oil were added at the expense of equal amounts of wheat starch. Fractions of cod-liver oil were prepared after saponification with potassium hydroxide in the presence of ethanol. The soap was split by the addition of hydrochloric acid and the resulting fatty acids washed and dried in a centrifugal separator. The fatty acids were then allowed to crystallize for 24 hr. at 15° C. and filtered through a bag filter at the same temperature. The fatty acid fractions were esterified with ethyl alcohol in the presence of sulphuric acid and the resulting esters refined, washed and dried under vacuum. The unsaponifiable matter was isolated by extracting a diluted solution of cod-liver oil soap with methylated ether. After three extractions, the solvent was removed from the washed extract by evaporation, the residue re-saponified and extracted with ether. The ethereal extract was then washed with dilute potassium hydroxide solution, followed by water washes until neutral, evaporated and dried under vacuum. The aqueous soap solution from which the unsaponified matter had been extracted was freed from dissolved ether, the soap split with acid and the fatty acids purified and esterified as above to give the fatty ester fraction free of unsaponifiable matter.

After feeding the experimental diets *ad lib.* over four weeks, the amount of total serum cholesterol of each rat was determined by the Liebermann–Burchard reaction.

The results presented (Table 1) show that the growth-rate was very poor, that is, only half that obtained on a stock ration. This may be ascribed to the sub-optimal protein content and the high fat content of the diet and to the presence of cholesterol and cholic acid. With corn oil in the diet, growth-rate was highest and somewhat higher than with cod-liver oil. The esterified fatty acid fractions caused a decrease in food intake which was paralleled by a slower growth-rate.

Table 1. MEAN GAIN IN WEIGHT, FOOD CONSUMPTION AND SERUM CHOLESTEROL

Addition to basal diet	Per cent	Daily weight increase (gm.)	Daily food consumption (gm.)	Total serum cholesterol (mgm./100 ml.)
Hydrogenated coconut oil	10	1·6	6·5	784
Corn oil	10	2·3	7·2	430
Cod-liver oil	10	2·1	7·0	196
Ethyl esters of fatty acids liquid at 2° C.; iodine value 189	10	1·6	5·9	241
Ethyl esters of fatty acids liquid at 15° C.; iodine value 161	10	1·7	6·3	240
Ethyl esters of fatty acids solid at 15° C.; iodine value 135	10	1·7	6·3	277
None		2·0	8·8	884
Cod-liver oil	10	1·7	6·6	205
Unsaponified matter	0·4	2·0	8·0	750
Ethyl esters of fatty acids	10	1·2	5·9	281
Unsaponified matter + ethyl esters of fatty acids	10	1·5	6·2	321

The serum cholesterol-level obtained with corn oil was much lower than with hydrogenated coconut oil. With cod-liver oil a significantly lower value was obtained than with corn oil ($P = 0{\cdot}003$ according to Wilcoxon's test). The ethyl esters of cod-liver oil fatty acids decreased the cholesterol content to nearly the same degree as did whole cod-liver oil. The mean serum cholesterol values obtained with the cod-liver oil fractions with different melting points were not significantly different. This may be the result of incomplete separation or of equal cholesterol-lowering properties of the various fatty acids present in the different fractions. The unsaponifiable fraction, in an amount equivalent to the level present in the whole cod-liver oil, exerted no distinct hypocholesterolemic action. The combination of unsaponified fraction with the esterified fatty acid fraction resulted in a mean value not significantly different from that obtained with whole cod-liver oil ($P > 0{\cdot}05$).

From these results it is concluded that cod-liver oil has a higher cholesterol-lowering activity than corn oil. The fatty acid fraction accounts for most if not all of the activity. The unsaponifiable fraction shows no distinct activity.

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Serological Relationships in the Genus *Gadus*

Little information is available concerning the serological relationships of fishes, and virtually nothing is known concerning the serology of the economically important genus *Gadus*.

Three species from this genus have been investigated in our laboratory, namely, the cod (*Gadus callarias* L.), the haddock (*G. aeglifinus* L.) and the pollack (*G. pollacius* L.). Blood was obtained from these three species by opening the animal after stunning, and taking it directly from the heart. The blood was allowed to clot, the serum separated, and merthiolate added to give a concentration of 1 : 10,000. The stock of rabbits used proved rather refractory, and the potency of the antisera was lower than might have been hoped. Three moderately satisfactory antisera were obtained, the first an anti-haddock serum *R* 71, and two anti-cod sera *R* 72 and *R* 712. Each of these antisera was produced after a course of intravenous injections of the fish serum. In the case of the anti-haddock serum, the intravenous course was followed, after a month's rest, by one series of intraperitoneal injections. In the case of the anti-cod serum, *R* 712, the second series of injections were subcutaneous. Anti-cod serum *R* 72 was produced by a single course of four intravenous injections. The amount used for each injection was 0·25 ml. of serum, and a course consisted of either three or four injections, given on alternate days. The characteristics of the antisera are shown in Table 1.

Table 1. Characteristics of the Antisera

Antiserum	Serum used from :	Reciprocal of homologous titre	Homologous photroner curve area
R 71	Haddock	1,000	107
R 72	Cod	1,000	84·5
R 712	Cod	10,000	92·8

The serological correspondence between the various species was determined using the photronreflectometer as described by Boyden and Delfaco[1]. The relationship ratios are given in Table 2. These ratios are calculated by expressing the area under the curve ($\sigma\tau$ value) of the second of the pair being compared as a percentage of the first. The reciprocal figures are also included (asterisks). Thus the cod/pollack ratios are derived from curves for antisera *R* 712 (100 : 21) and *R* 71 (27 : 100). The curves obtained from antiserum *R* 71 are shown in Fig. 1.

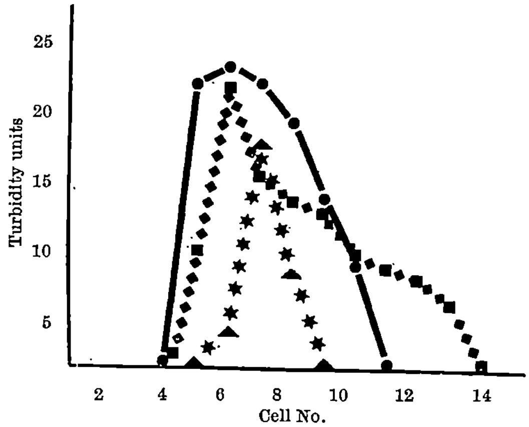

Fig. 1. ■, Haddock ; ◆, pollack ; ★, cod

Table 2. Relationship Ratios

	Antiserum used	Ratio	Mean
Cod / Haddock	*R* 712	100 : 24	25·3
	R 72	100 : 37	
	R 71	100 : 25*	
Cod / Pollack	*R* 712	100 : 21	24·0
	R 71	100 : 27*	
Haddock / Pollack	*R* 71	100 : 94	90·5
	R 712	100 : 87*	

* Reciprocal figures.

It will be seen that serologically haddock and pollack are closely related and that the cod is about equally remote antigenetically from both.

We are grateful to the Medical Research Council of Ireland for a grant to purchase the photronreflectometer used in these studies and to the Director, and Mr. R. J. Beverton, of the Lowestoft Fisheries Laboratory for sending fish sera and for enabling me to visit the Arctic in the summer of 1956 to collect the cod and haddock sera.

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Cephalotoxin : the Crab-paralysing Agent of the Posterior Salivary Glands of Cephalopods

The presence of a substance, toxic to crabs, in the posterior salivary glands of cephalopods (*Giftdrusen* of the German authors) has been known for a long time[1]. When a drop of saliva collected from *Octopus* is injected into a crab, a sequence of reactions is observed followed by complete paralysis of the animal[2]. Active substances have been extracted from the posterior salivary glands of octopuses[3], and their presence has been demonstrated in external and internal secretions[4]. Most of these substances have a powerful action on crabs and upon isolated organs of molluscs and other invertebrates[5]. Tyramine, the substance first isolated from the glands by Henze[6], was, and still is, believed to be the toxic agent[7]. However, none of the extractive substances found in the posterior salivary glands of cephalopods, even tyramine, can reproduce the paralysing action of the crude extracts or of saliva. The observations of Livon and Briot[8], recently confirmed by me[9], claim a more complex composition. The active principle is inactivated by heating, does not pass through dialysing membranes and can be purified by precipitation with ammonium sulphate.

From the posterior salivary glands of *Sepia officinalis* we have now purified a protein which, when injected into crabs, has the same effect as the dialysed extract from the same organ. The active protein has been called cephalotoxin.

As a measure of purification an arbitrary unit was taken which is defined as the amount of toxin which paralyses in 15 min. a crab weighing 40–50 gm. The animal used in all the experiments was the crustacean decapod *Eriphia spinifrons*. Control animals were injected with equal amounts of extract previously heated at 100° C. for 5 min. Specific activity was calculated as units per mgm. of protein. The protein content was determined colorimetrically with the Folin-phenol reagent[10].

After several attempts the simplest and easiest procedure for extraction and purification of cephalotoxin was found to be the following.

The organs are homogenized in a Waring blendor with 2 vol. cold 0·5 per cent potassium chloride, extracted for 4 hr. in the cold with continuous stirring and centrifuged at 800*g*. The precipitate is suspended again in 1 vol. potassium chloride solution, extracted, centrifuged as before and then discarded. The combined supernatants give: units per ml. 15; protein mgm. per ml. 23·0; specific activity 0·6. The extract is brought to *p*H 4 by careful addition of 2 *M* acetic acid. The precipitate is discarded by centrifugation at 15,000*g*. The supernatant is neutralized with 1 *N* sodium hydroxide and the new precipitate is centrifuged off and discarded. (Units per ml. 15; protein mgm. per ml. 14; specific activity 1·0.) The clear supernatant is dialysed against water for 24 hr. A white precipitate is formed which is discarded by centrifugation. (Units per ml. 15; protein mgm. per ml. 8·0; specific activity 1·9.)

The final extract can be concentrated in the cold or freeze-dried. The powder, redissolved in a small amount of water, gives a positive biuret and ninhydrin reaction and an ultra-violet absorption with a maximum at 276–278 mμ. After electrophoresis on starch gel[11] at *p*H 8·5, four bands are observed migrating towards the cathode. Further purification of the extract can be achieved by adsorption on calcium phosphate gel at neutral *p*H: three components are now visible after electrophoresis. Treatment with trypsin at 37° C. and neutral *p*H produces complete loss of the activity and disappearance of the bands within 3 hr.

Cephalotoxin can be extracted from the posterior salivary glands of *Octopus vulgaris* and *O. macropus* by a procedure similar to that described for *Sepia*.

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PLANT PHYSIOLOGY

Effect of Heavy Water on the Growth of *Chlorella vulgaris*

SEVERAL investigators have studied the effect of heavy water on the growth of algae[1–3]. All workers find that heavy water inhibits growth and, in concentrations approaching 100 per cent, no growth occurs. We have found recently that, while autotrophic growth of *Chlorella* is inhibited completely in 90 per cent (v/v) heavy water, growth on glucose, either in light or in darkness, is inhibited to a much smaller extent.

Chlorella vulgaris (Pearsall's strain) was grown in pure culture in medium buffered at *p*H 6·1[4]. Glucose was added, when required, in a final concentration of 1·0 per cent. The cultures were shaken at 25° C. either in darkness or in continuous light provided by fluorescent tubes giving a light intensity of 900 foot-candles. Growth was measured by a turbidometric method which was checked by hæmocytometer counts. Growth was exponential over several days and the growth constant, *k*, was calculated from $k = 24(\log_{10}n_2 - \log_{10}n_1)/t_2 - t_1$ where n_1 and n_2 are the number of cells present after t_1 and t_2 hours growth respectively.

When cultures containing glucose were shaken in light, growth was inhibited by heavy water. Not only was the rate of exponential growth reduced but also the lag period was increased (Table 1). Attempts to increase the growth-rate in 90 per cent heavy water by adaptation were unsuccessful, unlike those of Moses *et al.*[3]. In our experiments the growth-rate in 90 per cent heavy water was the same after three sub-cultures as it was originally.

Table 1. GROWTH OF *Chlorella vulgaris* IN DIFFERENT CONCENTRATIONS OF HEAVY WATER (D_2O)

Percentage D_2O (v/v)	Growth constant *k*	Approximate lag period (hr.)
0	0·70	20
50	0·46	20
70	0·35	150
90	0·20	160

The cultures contained 1·0 per cent glucose and were shaken at 25° C. in light of 900 foot-candles intensity.

In normal medium, *Chlorella* grows well in light without added glucose, and with our culture conditions, light stimulated growth even when glucose was added. However, when the medium contained 90 per cent heavy water, light inhibited growth; the cells grew fastest on glucose in darkness and illumination depressed the growth-rate. No autotrophic growth occurred at all (Table 2).

Table 2. EFFECT OF LIGHT ON THE GROWTH OF *Chlorella vulgaris* IN 90 PER CENT (v/v) HEAVY WATER (D_2O)

Glucose	−	+	+
Light	+	−	+
k—in normal medium	0·54	0·52	0·81
k—in medium with 90 per cent D_2O	0	0·23	0·17

The cultures were shaken at 25° C. The light intensity was 900 foot-candles. The concentration of glucose, when this was added, was 1·0 per cent.

The value of the growth constant, *k*, is given. Each value is the mean of two values obtained from two similar cultures.

Heavy water also had a marked effect on synthesis of chlorophyll. The illuminated cultures grown with glucose in 90 per cent heavy water were a bright orange colour. The pigments were extracted with ethanol and separated into carotenoids and chlorophylls. The absorption of the carotenoids was measured at 448 mμ and that of the chlorophylls at 660 mμ. These measurements indicated that the carotenoid content (per unit dry weight) of the orange cells was much the same as that of the normal cells but that the chlorophyll content was only one-fifth of normal.

Heavy water probably inhibits one of the dark reactions of photosynthesis[5,6]. In our experiments, the complete inhibition of autotrophic growth, which is entirely dependent on photosynthesis, compared with the partial inhibition of heterotrophic growth, indicates that the photosynthetic mechanism is more sensitive to heavy water than many other reactions. Nevertheless, reactions other than the photosynthetic ones are inhibited, and the fact that illumination reduces the growth-rate of cultures growing on glucose in 90 per cent heavy water suggests that a substance produced by the photolysis of heavy water is more inhibitory than heavy water itself.

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Effect of Phosphorylated Methyl-naphthohydroquinones on the Response to Radiation in Barley Roots

It has been shown by Mitchell and Simon-Reuss[1-3] that some phosphorylated methyl-naphthohydroquinones are radiosensitizers of radiation-induced mitotic inhibition in chick fibroblast tissue. It seemed possible that these chemicals might be of value in the induction of mutations in plants as they afforded a means of modifying response to radiation. Accordingly, experiments were carried out to see if any of these compounds are radiosensitizers in plant tissues.

Tetra-sodium 2-methyl-1 : 4 naphthohydroquinone diphosphate (compound 1) and tetra-sodium 2 : 3 dimethyl-1 : 4 naphthohydroquinone diphosphate (compound 28), both known to be radiosensitizers in animal tissues, were used in these experiments. X-rays were provided by a 220 kV$_p$. 'Maximar' unit working at 15 m.amp., giving radiation of wavelength 0·22 A. A 1-mm. aluminium filter was used. The nominal dose-rate was 156 r./min. at a distance of 20 cm.

Seeds of barley (var. Earl) were germinated on filter paper moistened with distilled water, in Petri dishes in light at a temperature of 20 ± 2° C. Germination was apparent after 24 hr. and seeds were selected for uniformity at this stage. They were transferred to Petri dishes with filter paper moistened with 2 ml. of the chemical, and 18 hr. later irradiated as described above.

With doses less than 300 r., mitosis is at a minimum 3 hr. after irradiation, and root tips were fixed in glacial acetic acid at this time for studying mitotic inhibition. This was done by hydrolysing root tips in N hydrochloric acid at 60° C. for 12 min. and staining with Feulgen's reagent. Root tips were squashed and counts made of the number of cells in the different stages of mitosis. The seedlings were grown in the Petri dishes for up to five days after irradiation, and each day 50 seedlings were analysed for weight and length of root and shoot.

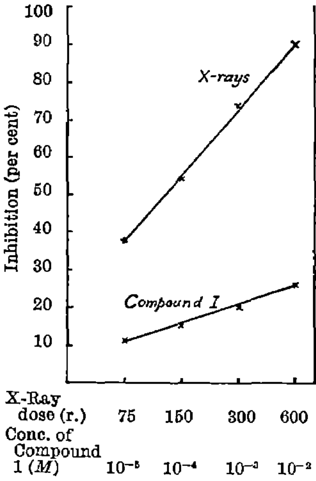

Fig. 1. Mitotic inhibition 3 hr. after irradiation

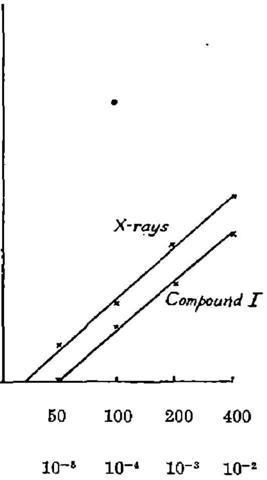

Fig. 2. Inhibition of increase of root fresh-weight 5 days after irradiation

Mitchell and Simon-Reuss[1] pointed out that to test for potentiation rigorously it is necessary to compare the effect of half-amounts of the two agents with the mean effect of the agents acting independently, and that there must also be a linear or sigmoid relation up to 50 per cent effect between response and dose for the separate agents. The effect measured with each of the agents acting alone should not be greater than 50 per cent. Figs. 1 and 2 show that there is a linear response to X-rays and compound 1 with mitotic inhibition 3 hr. after irradiation and with inhibition of weight of root five days after irradiation. Throughout these experiments the increases in weight and length of roots and shoots showed parallel responses to the treatments, so that only results for weights of roots are quoted.

Table 1 shows that compound 1 and X-rays have an additive effect on root growth five days after irradiation. Since growth is the product of many factors, it is not surprising that no potentiation can be demonstrated when measuring such a complex function. Five days after irradiation was chosen as the time to look for potentiation, as it is the earliest time at which the individual dose responses are linear. In fact, on the day after irradiation there is a stimulation of growth over the controls in all treatments, this effect gradually vanishing until on the fifth day the linear inhibition appears. Irrespective of the time after irradiation that root measurements were taken, no potentiation was observed. Compound 28 was not used for the experiments on growth measurements because of these difficulties of interpreting the results.

The examination of mitotic inhibition revealed the effects of the two chemicals and X-rays a short time after treatment, when responses should still be apparent and not masked as in the study of the increase of root weight and length several days after treatment. No measurements were made of chromosome abnormalities, but Bora[4] showed in broad bean roots that although these two chemicals do not cause chromosome breaks they increase the frequency of breaks induced by X-rays.

It is clear from Table 1 that compounds 1 and 28 have a radiosensitizing action on the mitotic inhibition induced by X-rays in barley roots. Both chemicals are themselves mitotic inhibitors, compound 28 being the more powerful. Compound 28 causes

Table 1

Treatment	Mitotic inhibition (per cent)	Potentiation factor	Treatment	Inhibition of fresh weight of root (per cent)	Potentiation factor
100 r. X-radiation	49·6		400 r.	49·1	
10^{-2} *M* Compound 1	26·7		10^{-2} *M* Compound 1	40·5	
5×10^{-3} *M* Compound 1	59·9	1·57 ± 0·16*	5×10^{-3} *M* Compound 1, followed after 18 hr. by 200 r.	46·1	1·03 ± 0·11
10^{-3} *M* Compound 28	38·8				
5×10^{-4} *M* Compound 28, followed after 18 hr. by 50 r. X-radiation	71·2	1·61 ± 0·18*			

* Significantly greater than 1 at 0·1 per cent level of probability. These figures are the means of five separate experiments.

metaphase accumulation, a finding which agrees with that of Mitchell and Simon-Reuss[2].

It appears from the above results that these two phosphorylated methyl-naphthohydroquinones act as radiosensitizers for mitotic inhibition in barley roots, and that this action is similar to that reported for chick fibroblasts in tissue culture and other animal tissues. Because they afford a means of modifying radiation response, they will be used to study the effect on X-ray induction of mutations in plants.

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Synthesis of Long-Chain Fatty Acids from 2-^{14}C-Acetate and ^{14}C-Glucose in *Trichoderma viride*

Although the synthesis of saturated fatty acids by the formal condensation of acetate units is well established, less attention has been paid to the formation of the common unsaturated acids (oleic, linoleic and linolenic) and their relationship to the saturated acids. The similarity in structure of oleic, linoleic and linolenic acids suggests a linked synthesis, and two processes have been considered: first a desaturation process leading from oleic via linoleic to linolenic acid, and secondly a hydrogenation process operating in the opposite direction. *Trichoderma viride*, a fungus which readily synthesizes palmitic, stearic, oleic, linoleic and linolenic acids, was chosen for studies with substrates labelled with carbon-14 in an attempt to obtain further information on the synthesis of unsaturated acids.

Mycelium was grown at 25° C. in a shaken 2 per cent glucose/acetate medium (*p*H 6·8), containing per litre: ammonium nitrate, 5·0 gm.; dihydrogen potassium phosphate, 3·5 gm.; crystalline magnesium sulphate, 2·5 gm.; ferric chloride, 0·08 gm.; zinc sulphate, 0·025 gm.; D(+)-glucose, 20·0 gm. and 5 ml. acetic acid neutralized with sodium hydroxide. After either two or four days growth the fungus was transferred to a single flask and equilibrated (4 hr.) with non-radioactive medium of similar salt composition containing, for the acetate experiments, 10 gm. D(+)-glucose and 0·25 gm. sodium acetate per litre, and for the glucose experiment 5 gm. D(+)-glucose and 0·125 gm. sodium acetate. At the end of this time 2-^{14}C-acetate or generally labelled ^{14}C-glucose was added, and after a suitable time the mycelium was removed by filtration and killed in boiling ethanol. Lipids were extracted in the usual way and the fatty acids obtained were separated by reversed-phase column chromatography[1], plated out and counted. Oleic and palmitic acids are not separable by this method, and the figure for palmitic acid was obtained from a second separation following removal of oleic acid after its conversion into short-chain acids by oxidation with alkaline permanganate. The figure for oleic acid was calculated by difference from that for the mixed oleic and palmitic acids.

The results in Table 1 show that radioactivity is incorporated into all the long-chain fatty acids within 3 hr. Closely similar results were obtained with 1- or 5-hr. periods. In every case the two saturated acids present (palmitic and stearic) and one of the unsaturated acids (oleic) had relatively high specific activities, whereas the other unsaturated acids (linoleic and linolenic) had much lower specific activities. This result obtained both in 2-day-old mycelium, which is rapidly synthesizing fatty acids, and in 4-day-old mycelium, in which fat synthesis is slow. Analysis of the free fatty acids (2·2 per cent of the total fatty acids), phosphatide fatty acids (41·4 per cent) and glyceride fatty acids (56·3 per cent) also showed the same distribution of radioactivity.

Table 1. Incorporation of Radioactivity into Long-Chain Fatty Acids after 3 hr. Growth on 2-^{14}C-Acetate or Generally Labelled ^{14}C-Glucose

Fatty acid	Age of mycelium and radioactive substrate					
	2-day glucose		2-day acetate		4-day acetate	
	c.p.m./mgm.	gm./100 gm. fatty acid	c.p.m./mgm.	gm./100 gm. fatty acid	c.p.m./mgm.	gm./100 gm. fatty acid
Palmitic	508	20·9	9,628	20·9	1,129	21·3
Stearic	367	5·4	2,570	5·4	940	5·6
Oleic	329	29·0	7,509	29·0	701	24·0
Linoleic	53	42·3	1,522	42·3	149	44·0
Linolenic	65	2·2	434	2·2	48	5·0
Total c.p.m. supplied	$54 \cdot 3 \times 10^6$		$17 \cdot 4 \times 10^6$		$14 \cdot 5 \times 10^6$	

These results indicate clearly that oleic acid is the first of the unsaturated acids to be formed and give little support to the hydrogenation hypothesis in which it is assumed that the most unsaturated acid is formed first. In view of the fact that similar results were obtained using either radioactive glucose or radioactive acetate as a carbon source it also seems unlikely that triose units are involved, as has been suggested, in the synthesis of unsaturated acids. A more probable explanation of the results would be that glucose is broken down into C_2 units before its incorporation into fatty acids.

In a further experiment 2-day-old mycelium, after being fed for 3 hr. with 2-^{14}C-acetate (see Table 1), was transferred, after careful washing, to a similar but non-radioactive medium for a further 2 days. During this time mycelium dry weight and lipid weight approximately doubled. At 4 days the material was harvested, and the following specific activities (c.p.m./mgm.) were obtained: palmitic acid, 9,612; stearic acid, 2,924; oleic acid, 6,406; linoleic acid, 5,939; and linolenic acid, 2,309. None of the fatty acids showed any significant decrease in specific activity, and this is accounted for by the fact that there was a rise in the total count in the fatty acids from $44 \cdot 9 \times 10^4$ c.p.m. at 2 days to $72 \cdot 2 \times 10^4$ at 4 days. This could be the result of insufficient washing at the 2-day stage or it may be caused by the formation of a 'pool' of radioactive precursor within the tissue[2]. It is interesting, however, that whereas the specific activities of palmitic, stearic and oleic acids show only a small change, those of linoleic and linolenic acids have increased severalfold. This again indicates that these acids are formed later than oleic acid, and is consistent with synthesis by successive dehydrogenation of oleic acid, although other explanations cannot be dismissed on the present evidence. These results will be reported and discussed in detail elsewhere.

We are most grateful to Dr. D. W. Turner (Department of Chemistry, Imperial College, S.W.7) for access to a proportional counter and for guidance in its use.

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Effects of Gibberellic Acid on Winter Pasture Production

The problem of restricted winter growth of pastures is of agronomic importance in many countries. This is especially true over large areas of Australia where fodder conservation, as one solution, is not economic. The possibility, inherent in the work of Morgan and Mees[1,2], Leben and Barton[3], Wittwer *et al.*[4,5] and Corns[6], that gibberellic acid might increase winter growth of continuously grazed pastures, does not appear to have been exploited beyond an initial experiment of Scurfield and Bull[7]. Results of that experiment were sufficiently encouraging to warrant our pursuing the matter further.

Experiments were carried out during the winter of 1958 on grazed pasture of *Phalaris tuberosa* and *Trifolium subterraneum,* sown twelve years previously. Four sites were chosen at random and, within each of these, four sub-sites. On each sub-site, sixteen plots (each of four sq. lk.) were located at random (subject only to the restriction that each had complete foliage cover). In each group of sixteen plots, four at random received nitrogen (as ammonium sulphate =224 lb./acre), four an aqueous solution of gibberellic acid (=3·69 oz./acre), four gibberellic acid plus nitrogen, and four were untreated (controls). Prior to treatment, all plots were clipped to ground-level. After treatment, they were clipped to this level on four occasions: the harvest data (lb. dry matter per acre) are given in Table 1.

Compared with controls, plots treated with gibberellic acid produced a greater yield of both grass and clover at harvests I and II, an equivalent yield of grass and a lesser yield of clover at harvest III, and a lesser yield of both at harvest IV. Over the four harvests so far taken, there was a significant increase in total yield of dry matter. This result confirmed that obtained previously[7], but not that of Morgan and Mees[1,2]. They found, after applying gibberellic acid (=2 oz./acre) to pastures at various times from spring to autumn "in no case any net increase of yield over two or more cuts". More interesting, however, than an overall increase in yield was the stimulation of growth at a time of normally slow growth. Continuous meteorological records kept for the site showed that this alteration could be achieved under conditions of adequate rainfall and minimum temperatures as low as −9·5° C. (grass) and −4·5° C. (screen) (compare the records of Leben and Barton[3] and Wittwer and Bukovac[4]).

Changes in the botanical composition of the harvested material were of interest. Treatment with gibberellic acid caused a significant ($P < 0 \cdot 05$) depression of percentage clover in the material harvested on the second and third occasions. How far this was a direct effect of gibberellic acid and how far it reflected an altered competitive status of the species present was uncertain. The result failed to confirm that of Morgan and Mees[2], who found treatment with gibberellic acid to cause no change in the botanical composition of swards over a period between treatment and a third cut.

There were significant ($P < 0 \cdot 001$) reductions in percentage total nitrogen of *P. tuberosa* (from 4·25 to 3·66 at harvest I, 5·37 to 4·13 at harvest II and 4·57 to 4·20 at harvest III) as a result of gibberellic acid treatment. This confirmed earlier results[1–3,7] (not, however, those of Wittwer *et al.*[5]) obtained with other grasses. Despite such reductions, the total yield of nitrogen (Table 1) over all four cuts was significantly greater from plots treated with gib-

Table 1. Effects of Gibberellic Acid and Nitrogen on Dry Matter Production (lb./acre), Percentage Clover in Total Dry Matter and Yield of Nitrogen (lb./acre) from *Phalaris tuberosa—Trifolium subterraneum* Pasture
Mean of 64 plots at each harvest.

Treatment (applied July 10, 1958)	Harvest I (July 24, 1958)			Harvest II (Aug. 14, 1958)			Harvest III (Sept. 11, 1958)			Harvest IV (Oct. 16, 1958)			Total (4 harvests)	
	Grass	Clover	Clover (per cent)	Grass	Clover	Clover (per cent)	Grass	Clover	Clover (per cent)	Grass	Clover	Clover (per cent)	Dry matter	Yield of nitrogen
Control	82	9	10·2	176	51	22·5	308	136	30·6	890	834	48·4	2,486	92
+ Gibberellic acid	416*	68*	14·1	499*	102†	17·0‡	317	104‡	24·7‡	665*	538*	44·7	2,709†	98*
+ Nitrogen	68‡	7‡	9·8‡	226‡	42	15·5†	412*	101*	19·6*	1,042*	617†	37·2‡	2,515	—
+ Gibberellic acid + nitrogen	358*	35*	9·0	568*	63	10·0*	347‡	69*	16·6*	744*	417*	36·0‡	2,601	—

Degree of significance shown by: $*P < 0 \cdot 001$, $\dagger P < 0 \cdot 01$, $\ddagger P < 0 \cdot 05$.

berellic acid than from control plots. Analyses have so far failed to demonstrate any similar effect of gibberellic acid on the nitrogen content of the clover.

The leaf 'burning' caused by the added ammonium sulphate makes the interpretation of the yield results from such plots somewhat uncertain, but evidently the quantitative effects of added nitrogen upon yield did not resemble those of gibberellic acid. Regarding the effects of nitrogen and gibberellic acid added together, no evidence of interaction between the two in relation to total yield was obtained. It was noted that both *Phalaris tuberosa* and *Trifolium subterraneum*, irrespective of simultaneous nitrogen application, showed chlorosis and other symptoms of gibberellic acid treatment[8,9], though by harvest IV chlorotic symptoms at least had disappeared.

An initial grazing experiment using Merino wethers on a similar pasture to the above has so far: (*a*) confirmed that treatment with gibberellic acid (=1·6 oz./acre) could increase late-winter pasture growth and (*b*) provided no evidence of a deleterious effect of herbage so treated on either the health or live weight of sheep after two months grazing. This latter fact supports the finding of Peck *et al.*[10] that gibberellic acid, administered in various ways directly to small animals, was non-toxic.

The results of the above experiments will be considered more fully elsewhere.

We are grateful to Mr. G. A. McIntyre for the statistical analysis of the data in Table 1.

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Geotropic and Morphological Alterations in Rice Seedlings caused by Plant Growth Regulators

During some investigations into the effects of gamma-BHC on rice seeds a number of experiments were carried out to test whether BHC was behaving in a similar way to plant growth substances in producing abnormalities. These experiments were carried out because it was found that gamma-BHC inhibited root growth at low concentrations (for example, in aqueous solutions at 10^{-5} *M*, root growth was reduced to half that of the controls) and because of a recent suggestion by MacLagan[1] that some of the chlorinated hydrocarbons, including BHC, might behave in a similar way to auxins in plant tissue. It has now been found (unpublished work) that BHC does not behave as an auxin so far as rice seedlings are concerned. Nevertheless, during these experiments some results were obtained which may shed some light on current theories of geotropism and also on the effects that auxins have on morphogenesis.

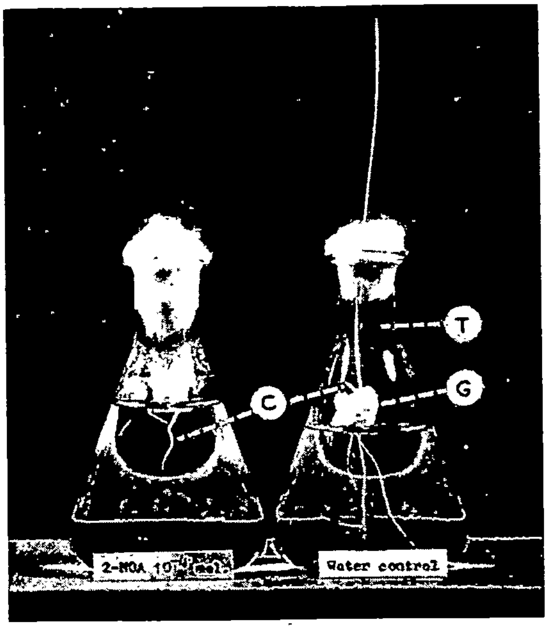

Fig. 1. Rice seedlings 7 days old growing in 10^{-4} *M* 2-naphthoxyacetic acid (left) compared with control (right). *C*, coleoptile. The apparatus consists of a 100-ml. conical flask containing 100 ml. of the test solution; the seed is held at the surface of the solution in a 10-mm. bore glass tube (*T*) the end of which is covered by cotton gauze (*G*); a cotton-wool plug holds the tube in position

Rice seedlings were germinated and grown for seven days in the apparatus shown in Fig. 1. The seeds were held at the surface of aqueous solutions of substances which have auxin activity and 'anti-auxins'; distilled water was used as control. Ten replicates were used for each treatment. Linear growth measurements and photographic records were made at the end of the experimental period. The substances with auxin activity were β-indolylacetic acid, naphthalene-1-acetic acid, methyl*iso*butylcarbonyl ester of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T MIBC ester) (a crude preparation containing 71 per cent w/w) and 2-naphthoxyacetic acid. The substances used which are usually classed as anti-auxins were 1-naphthoxyacetic acid, 2,3,5-tri-iodobenzoic acid and α-(1-naphthylmethylsulphide)-propionic acid.

All the substances with auxin activity showed very similar effects on the seedlings though the concentrations necessary for the various effects differed. The three most obvious effects were inhibition of root growth, the production of an epicotyl (not present in the controls) and the reversal of shoot geotropism. The lowest concentrations required to produce an epicotyl and reverse shoot geotropism were as follows: 10^{-3} *M* indolylacetic acid, 10^{-4} *M* 2-naphthoxyacetic acid, 10^{-5} *M* naphthalene-1-acetic acid and 10^{-6} *M* 2,4,5-T MIBC ester. At these concentrations at least 60 per cent of the coleoptiles showed complete reversal of geotropism on all three occasions when these substances were tested. The epicotyls produced at these concentrations were 2–4 mm. long. In a large number of germination tests carried out in this laboratory on moistened filter paper or sand

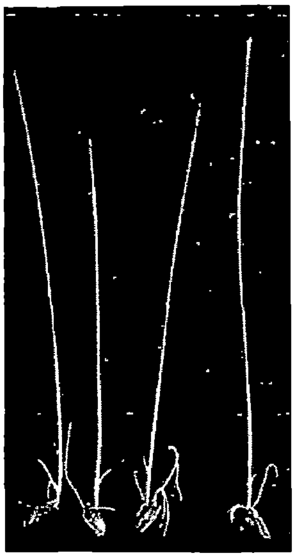

Fig. 2. Photograph of 7-day old rice seedlings showing the reversal of root geotropism caused by 10^{-4} *M* 1-naphthoxyacetic acid. Note that secondary roots have the normal positive geotropic response

trays both in the light and in the dark there has never been any evidence of the production of an epicotyl. However, additional experiments have now been carried out in which rice seeds were placed in beakers and submerged beneath various depths of water from 3 to 10 cm.; under these germination conditions in the dark, epicotyls 4–6 mm. long were produced, but under the same conditions in diffuse daylight no epicotyls were found. Continuous aeration of the water in the case of submerged-germination tests in the dark decreased the size of the epicotyls to 2–4 mm. It would seem, therefore, that an epicotyl is normally produced under dark, poorly aerated conditions, but that high concentrations of substances with auxin activity are capable of inducing its formation even under light, well-aerated conditions. Microscopic examination of transverse sections showed that there were no distinguishable anatomical differences between epicotyls produced by the dark, poorly aerated conditions or by application of substances with auxin activity. This similarity would be expected if epicotyl formation is due to a rise in auxin concentration. Yamada[2] has shown that rice coleoptiles grow to a greater length under water than in the air, and has presented evidence which suggests that this is due to the reduced capacity of the tissues to destroy auxin when submerged; submersion, he found, was equivalent to a 20–30-fold increase in indolylacetic acid. The absence of an epicotyl in the light, even in submerged seedlings, would fit in with the demonstrated presence in plant tissues of the light-stimulated indolylacetic acid oxidizing system, originally shown by Galston[3] in etiolated pea epicotyls.

One of the most general effects of the substances with reputed anti-auxin activity was inhibition of root growth at and above the following concentrations: 10^{-5} *M* 1-naphthoxyacetic acid, 10^{-8} *M* 2,3,5-tri-iodobenzoic acid, and 10^{-8} *M* α-(1-naphthylmethylsulphide)-propionic acid. In this way they showed a similarity with the auxins, but unlike the experiments with auxins, there was never any evidence of an epicotyl being induced to form. Neither α-(1-naphthylmethylsulphide)-propionic acid nor 1-naphthoxyacetic acid reversed coleoptile geotropism, though 2,3,5-tri-iodobenzoic acid did cause a positive response in approximately 20 per cent of the seedlings at 10^{-6} and 10^{-7} *M*. The most interesting result was obtained with 10^{-4} *M* 1-naphthoxyacetic acid: when seeds were grown at the surface of a solution of this strength, 60 per cent or more of the seedlings showed a reversal of root geotropism, and the roots grew upwards into the air away from the solution (Fig. 2). In the cases where root geotropism was reversed, the roots were strongly inhibited and showed only 20–30 per cent growth compared with the controls. This reversal of root geotropism was obtained on all three occasions when this concentration of 1-naphthoxyacetic acid was tried.

These results are considered to support the classical theory of geotropism in which it is postulated that the shoot contains sub-optimal concentrations of auxin, whereas the roots contain optimal or supra-optimal concentrations. It follows that if the effective concentration of auxin in the shoot is raised to a supra-optimal level it should behave geotropically as a root; conversely, if the effective concentration of natural auxin in the root is reduced—for example, by an anti-auxin—to a sub-optimal level, then the root should behave as a shoot. It is interesting to note that out of the five 'anti-auxins' which Street[4] tested, 1-naphthoxyacetic acid was the most effective in counteracting the effect of a natural auxin which accumulates in excised tomato roots and causes 'ageing'. It may be significant, therefore, that 1-naphthoxyacetic acid was the only substance used in the present investigations which reversed the geotropism in rice roots.

These results will be discussed more fully in a later publication.

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Prolonging Dormancy in *Vitis vinifera* with Gibberellin

At Davis, California, grape buds developing on the basal portions of shoots normally enter a dormant stage about September. By the following April the buds usually begin rapid growth. Both a small amount of cold and a certain interval of time are required for dormancy to break. If the dormant buds could be made to grow in the autumn, the crop of the following year could be estimated. Since gibberellin has been reported to break the dormancy of buds in peach[1] and potato[2,3], and of epicotyls in the tree peony[4], it was tested for this purpose on grapes.

The potassium salt of gibberellic acid, supplied by Merck and Co., contained about 80 per cent active ingredient.

In one experiment, Zinfandel vines were sprayed with gibberellin at 0, 10, 50 or 250 p.p.m. on September 6, 1957, two vines per treatment. At this time the foliage was still green and the percentage of total

Table 1. GROWTH OF SHOOTS ON APRIL 19, 1958, ON ZINFANDEL VINES SPRAYED THE PREVIOUS AUTUMN WITH GIBBERELLIN

Concentration of gibberellin (p.p.m.)	Average length per shoot (in.)	No. of shoots per vine on spurs	No. of water sprouts* per vine
0	3·0	18	56
10	1·7	14	34
50	1·7	3	8
250	1·6	1	2

* Water sprouts refer to shoots arising from wood more than one year old.

soluble solids of fruit was about 20. After the leaves had fallen, in November, buds in all treatments were still dormant. In January 1958 vines were pruned to 9–11 spurs, each bearing 2–3 buds[5]. On April 19, control shoots were about 3 in. long (Table 1). The number of shoots decreased with increasing concentration of gibberellin, indicating that dormancy had been prolonged by gibberellin. Results were comparable in an experiment with the Tokay variety.

In a second type of experiment, cuttings of Tokay canes about 16 in. long were taken from the vineyard on December 4, 1957, and placed in a greenhouse with their bases in solutions containing 0, 0·01, 0·1, 1, 10 or 100 p.p.m. of gibberellin. The solutions, about 3 in. deep, were changed each week. There were thirty cuttings per treatment. At later intervals the cuttings were examined to see whether buds had begun growth. A cutting was said to have initiated growth when green was visible on one or more buds of a cutting. The results (Table 2) show that the higher the concentration of gibberellin, the longer the development was delayed. With one exception, no buds began growth by February 20 on cuttings placed in gibberellin in the range 1–100 p.p.m. This experiment was repeated with other sets of cuttings after they had been stored at a temperature of about 32° F. for two, four or six weeks. The trends were similar.

Table 2. NUMBER OF TOKAY CUTTINGS OUT OF THIRTY THAT SHOWED BUD GROWTH ON VARIOUS DATES AFTER BEING PLACED IN SOLUTIONS OF GIBBERELLIN ON DECEMBER 4, 1957

Concentration of gibberellin (p.p.m.)	Date of readings		
	Jan. 23, 1958	Feb. 6, 1958	Feb. 20, 1958
0	7	9	17
0·01	3	8	17
0·1	1	5	13
1	0	0	0
10	0	0	0
100	0	0	1

It is of interest that gibberellin prolongs dormancy of buds of *Vitis vinifera* despite the fact that growth of shoots is greatly stimulated[6]. Gibberellin may be of use for retarding bud break in the spring in regions of early frosts.

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BIOLOGY

Acquired Immunological Tolerance of Heterografts

ACQUIRED immunological tolerance of heterologous cells is of much lower degree than tolerance of homologous cells[1]. In experimental embryonal parabiosis[2], a large quantity of powerful antigenic stimulus is administered; this acts for a relatively long time during the 'adaptive period' and usually results in the formation of cell chimeras. A relatively high degree of heterologous tolerance was sometimes obtained by this method, for a prolonged survival of heterografts has been found in turkey–chicken parabionts[1], and an interspecific blood chimera demonstrated[3].

The degree of tolerance to heterografts has now been studied in further turkey–chicken parabionts. In one turkey parabiont, a chicken skin graft survived for three months and grew feathers. No chicken erythrocytes were demonstrated during this period in the turkey's blood. It is possible that no erythrocyte chimera was formed in this parabiont, or that, if it was formed, it disappeared from causes other than the immune reaction.

Skin heterografts from two chickens were applied to one turkey parabiont with persistent erythrocyte chimerism at the age of one year. Neither of the donors was the partner in the embryonal parabiosis. The grafts survived for 80 days, when the recipient died. A skin homograft from a turkey had been applied at the same time. This also survived for the whole 80 days. In control turkeys, skin homografts survive for only 10–14 days. Gamma-globulins were demonstrated by paper electrophoresis in the serum of this parabiont; it was therefore not a case of agammaglobulinæmia. Moreover, a guinea-fowl heterograft was destroyed by the turkey in the normal time. Immunological reactivity against heterografts from other species was thus maintained.

This example of a high degree of heterologous tolerance shows that in tolerance between turkeys and chickens, the immune reaction against individual antigenic differences within the donor species is lost, as well as its response to the individual antigens of the recipient's own species.

We then studied the occurrence of interspecific blood chimerism in turkey–chicken parabionts. Agglutination by specific antiserum revealed the presence of turkey erythrocytes five weeks after hatching in six chicken parabionts out of eight, and in four seven weeks after hatching. In one chicken, turkey erythrocytes were present up to the tenth week after hatching. Taking into account the length of the life of avian erythrocytes[4], most of these cases cannot represent a mere survival of the partner's erythrocytes exchanged during embryonal parabiosis, but must involve a repopulation by the partner's transplanted hæmatopoietic cells. They are therefore interspecific erythrocyte chimeras.

In one turkey, chicken erythrocytes were demonstrated up to the time of the bird's death at the age of 14 months, and actually comprised the majority of its erythrocytes. Chicken erythrocytes were also demonstrated in a specimen of blood taken after death.

The question arises whether this may not have been a case of pseudochimerism, as observed in avian bird embryos after transplantation of adult spleen cells[5]. Transplantation of prospectively immunologically active cells from the chicken parabiont to the turkey partner might have occurred during embryonal

Table 1

Plasma taken :	Chicken plasma No.:	Erythrocytes of chicken No.: 728	734	882	883	885	886	2911	Titre of anti-turkey hæmagglutinins
Before immunization	2120	–/–	–/–	–/–	–/–	–/–	–/–	–/–	8
	2300	–/–	–/–	–/–	–/–	–/–	–/–	–/–	4
After immunization	2120*	+/++	+/+++	+/++	+/+	+/+++	+/+++	+/++	128
	2300	–/–	–/–	–/–	–/–	–/–	–/–	–/–	64

Chick No. 2120 immunized with blood of chimeric turkey parabiont (age one year). Chick No. 2300 immunized with blood of control turkey. Citrated plasma used for agglutination reactions undiluted, if not stated otherwise. Isoagglutination read after 30 min./24 hr.; titre of anti-turkey hæmagglutinins determined after 30 min.

* Plasma diluted 1 : 10.

parabiosis. These cells could probably acquire tolerance to the host's antigens. Later in life, however, they might lose this tolerance and form antibodies against turkey agglutinogens, which would then combine with the host's erythrocytes. Agglutination of these sensitized turkey erythrocytes by antiserum against chicken blood would thus simulate the presence of chicken erythrocytes—a case of pseudochimerism. In order to exclude this possibility, chicken agglutinogens were demonstrated in the blood of this chimera by means of immunization. Chickens do not possess natural agglutinins and do not form them even when immunized with turkey blood. Immunization of chickens with the blood of the chimera, however, resulted in the formation of *iso*agglutinins which also agglutinated the erythrocytes of other chickens in a relatively high titre (Table 1). Individual chicken antigens must have been present in the blood of the chimera to induce the formation of these antibodies. The demonstration of chicken antigens thus showed that this was actually a case of prolonged interspecific chimerism.

Table 2

Serum	Titre of serum: Non-absorbed	Absorbed: With normal erythrocytes of turkey No. 41	With normal erythrocytes of chicken No. 735	With erythrocytes released after agglutination with chicken isoimmune serum of turkey No. 10/11 (chimera)	With erythrocytes released after agglutination with chicken isoimmune serum of chicken No. 725
Against turkey erythrocytes	16	< 4		16	
Against chicken erythrocytes	16		< 4		< 4

Plasma diluted 1 : 2 and absorbed with equal volume of 33 per cent erythrocyte suspension (final dilution 1 : 4).

Another question investigated was whether erythrocytes with *both* chicken and turkey antigens occurred in the turkey chimera, in addition to chicken and turkey erythrocytes. Erythrocytes of the chimera were exposed to antisera against chicken erythrocytes. Clumped erythrocytes were separated from free cells by differential centrifugation, thus separating erythrocytes with chicken agglutinogens from those without them. The clumps were then broken up mechanically. Although the cells were free in physiological saline, they agglutinated in any serum, including their own. It was thus an example of the agglutination of sensitized erythrocytes in a protein medium. An attempt was therefore made to demonstrate turkey agglutinogens in these cells by absorption of chicken serum against turkey blood. This, however, did not reduce the agglutinin titre (Table 2). Erythrocytes containing turkey and chicken agglutinogens simultaneously were thus not demonstrated in the blood of this chimera by the method used in the present experiment.

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Antibody Formation in Tissue Culture

While the production of antibodies by explanted tissues or cells from immunized animals is readily demonstrable, most attempts to initiate antibody formation *in vitro* have met with failure. Only recently has the original claim for success[1] been substantiated by the observations of Stevens and McKenna[2], who found that normal rabbit spleen produced antibody to bovine γ-globulin after exposure to this antigen *in vitro*, but only if either the rabbit or the spleen had previously been treated with *S. typhi* endotoxin.

This report describes the *in vitro* initiation and production of two different antibodies in cultivated lymph node cells of normal rats: one reactive with the bacteriophage *T*2, the other with hæmocyanin (busycon canaliculum). In order to induce the formation of the *T*2 antibody, it was necessary first to expose the virus to the cells of a rat peritoneal exudate obtained 48 hr. after intraperitoneal injection of beef infusion broth[3]. These cells (90 per cent macrophages) were washed once with buffered saline and then were packed by centrifugation. The packed cells (approximately 1·4 × 10^8) were suspended in 5 ml. buffered saline containing 10^3 *T*2 phage. The mixture was incubated at 37° C. for 30 min. The cells were then sedimented by centrifugation at 1,000 r.p.m., washed twice with buffered saline, ground in a Ten Broeck homogenizer and passed through a Seitz filter.

2 ml. of this cell-free filtrate were distributed among eight Esmarch dishes which contained rat lymph node cells maintained in Trowell's synthetic medium[4]. Preparations of untreated bacteriophage in comparable dilution, and of suspensions of normal rat macrophages alone, were added to other lymph node cultures. The plates were incubated at 37° C. under a 4 per cent carbon dioxide atmosphere. The supernatant fluids from these cultures were removed after varying periods of time and to one volume of fluid was added one volume of saturated ammonium

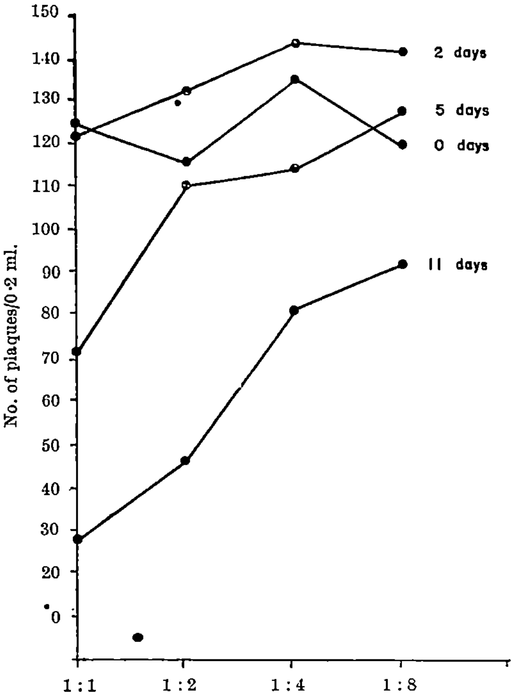

Fig. 1. Effect of length of incubation on the formation of *T2* bacteriophage neutralizing antibody from rat lymph node cell tissue cultures exposed to rat macrophage-treated *T2* bacteriophage

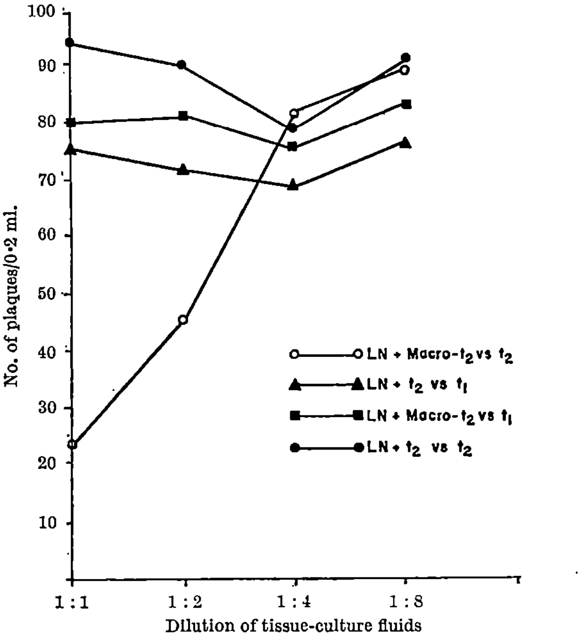

Fig. 2. Neutralization of *T1* or *T2* bacteriophage by fluids from rat lymph node cell tissue cultures exposed to either *T2* bacteriophage or rat macrophage-treated *T2* bacteriophage

sulphate. The resulting precipitate was dissolved in one-eighth the original volume and dialysed overnight against buffered saline of *p*H 7·6. These concentrated fluids were tested for phage neutralization by adding dilutions of the fluid to constant numbers of *T2* phage, incubating for 30 min. at 37° C., plating on *E. coli B*, and counting plaques after 24 hr.

Phage neutralization was found only with fluids from lymph-node cells that had been exposed to macrophage-treated phage particles. As may be seen in Fig. 1, the neutralizing substance appeared on the fifth day and increased in titre to the eleventh day, after which the cells began to lose viability. Fluids which neutralized *T2* did not neutralize *T1* as shown in Fig. 2. The pretreatment of the virus by rat macrophages could not be replaced by treatment with rabbit macrophages or with HeLa cells. It was also found that the treatment of the phage with rat macrophages which had been damaged by freezing and thawing or by exposure to the Mickle vibrator was ineffective. However, a homogenate from rat macrophages prepared by the use of a Ten Broeck grinder could be substituted successfully for intact macrophages.

A primary antibody response to hæmocyanin was induced in lymph-node cells from normal rats by the addition to the culture of a cell-free filtrate from a mixture of hæmocyanin and rat macrophages (0·25 mgm. nitrogen/ml. hæmocyanin and approximately $1 \cdot 4 \times 10^8$ cells were used). Hæmocyanin alone again failed to elicit antibody formation. The titres of concentrates of tissue culture fluids, prepared in the same manner as above, are shown in Table 1. The hæmagglutination method of Boyden[5] was employed. If the tissue-culture fluids were freed of protein with perchloric acid, hæmagglutination activity was lost.

Table 1. HÆMAGGLUTINATION TITRES OF TISSUE CULTURE FLUIDS AGAINST HÆMOCYANIN

Post-incubation time (days)	Hæmagglutination titres Antigen added to rat lymph node tissue cultures	
	Hæmocyanin	Macrophage-treated hæmocyanin
0	0†	0
4	0	0
7	0	1 : 10
11	0	1 : 80–1 : 160

† Titre less than 1 : 10.

Further work is under way to characterize the *T2* phage-neutralizing substance.

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Glutamine Metabolism of Normal and Malignant Cells cultivated in Synthetic Media

PREVIOUS communications from this Laboratory[1,2] have reported changes in the amino-acid content of synthetic medium *M* 150 during cultivation of a variety of freshly explanted tissues and have established a characteristic pattern of change with each tissue studied[3]. Cultivation of strain *L* (Earle) cells of mouse fibroblastic origin revealed a pattern of changes in the synthetic medium differing significantly from that of the freshly explanted tissues in regard to the metabolism of glutamine[4]. These studies have now been extended to a number of cell lines of malig-

Table 1. CHANGES IN GLUTAMINE CONCENTRATION OF SYNTHETIC MEDIUM DURING CULTIVATION OF VARIOUS CELLS AND TISSUES

Tissue cultures	Change in glutamine content of medium*
Chick embryonic heart	+ + +
Chick embryonic kidney	+ +
Chick embryonic liver	+ +
Monkey kidney explants	+
Monkey kidney trypsinized	–
Strain *L* (mouse fibroblasts)	– –
HK 55 (human kidney)	– –
FL strain (human amnion)	– –
Strain HeLa (human malignant epithelium)	– – –
J-96 (human leukæmic)	– – –
J-111 (human leukæmic)	– – –
J-128 (human leukæmic)	– – –

* +, Increase –, decrease. Changes are based on most active period of metabolism of each culture type.

nant origin and appear to have established a consistent difference between the two types of cultures. All cultures of freshly explanted tissues so far examined accumulate glutamine in the culture medium, while all established cell lines studied utilize this amide from the surrounding fluid.

The composition of the synthetic medium and the methods of tissue cultivation have been described previously[1–5]. Samples of the culture medium were removed at appropriate intervals, pooled, and aliquots analysed by paper chromatography[1,2], using both one-dimensional and two-dimensional methods for separating completely the amino-acids of the culture medium. The results of these experiments are summarized in Table 1.

It is evident that the freshly explanted tissues show a marked increase in the glutamine content of the medium. On the other hand, the established cell strains, which are largely of human malignant origin, bring about a marked decrease in the glutamine concentration. This decrease is greatest with the HeLa cell strain and the three lines of human leukæmic cells, while the human kidney, human amnion, and strain *L* cells show the same change to a lesser degree. The behaviour of monkey kidney cells appears to depend on the method of preparation of the cultures. Primary cultures prepared from freshly explanted fragments cause a slight increase in glutamine content of the medium, while primary cultures prepared by trypsinizing the tissue to a cell suspension bring about a slight decrease in glutamine concentration. Similar variation in glutamine metabolism by monkey kidney cells cultivated in media supplemented with serum has been observed by Eagle *et al.*[6].

The completely synthetic medium used in these experiments supports the survival of freshly explanted tissues for more than 30 days and maintains the established cell strains for somewhat shorter periods. The results presented in Table 1 were obtained, therefore, under conditions of survival and active metabolism, but not of rapid propagation. It should also be noted that synthetic medium *M* 150 contains a high level of glutamic acid in addition to glutamine, but that the changes in glutamine content of the medium have been demonstrated previously[4] to be independent of glutamic acid.

The present observation that established cell strains, of predominantly malignant origin, reduce the glutamine content of the culture medium is in accord with the report by Roberts and Borges[7] that tumour cells are generally distinguishable from normal tissues by their low levels of free glutamine. It should also be pointed out that the present status of the established cell strains is somewhat uncertain. Those now available, whether of normal or malignant origin, appear to possess certain malignant characteristics, and it is considered that alterations in cell type or properties have occurred during the period preceding their establishment as cell lines[8,9]. The present observation that such cell lines can utilize glutamine may be interpreted, accordingly, either as a possible metabolic difference between normal and malignant cells, or as a possible alteration in cell metabolism associated with the establishment of permanent cell lines in tissue culture.

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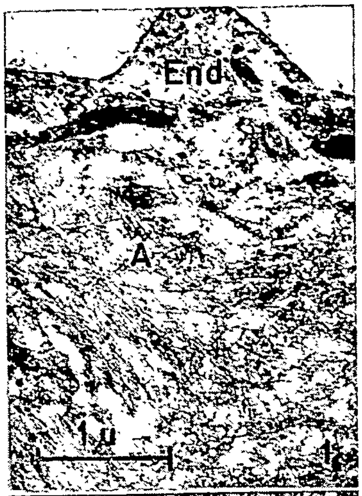
Electron Microscopic Observations on a Fibrous Component in Amyloid of Diverse Origins

AMYLOIDOSIS in man and animals may be associated with other disease entities or may occur spontaneously. The relationship, if any, of the different forms of amyloid has proved difficult to ascertain, and the chemical nature of amyloid has not been established. Previous studies have indicated that it is predominantly protein in nature[1,2] and have suggested that the protein is not primarily collagen[3] or γ-globulin[4]. No chemical differences have been noted in amyloid of different sources. The precise definition of the amyloid protein has, however, been hampered by its insolubility in organic solvents.

Polarization microscopy in this laboratory as in others[5] has demonstrated that unstained and congo red stained accumulations of amyloid of a variety of sources exhibit positive birefringence with respect to the long axis of the deposit. This suggests that amyloid is not as structurally amorphous as it appears in the light microscope. To explore this possibility, electron microscopic studies were undertaken.

The following materials were used: (1) kidneys of 6 rabbits with casein-induced amyloidosis obtained immediately at the time of killing; (2) skin and subcutaneous tissue biopsy material from a patient with proved primary amyloidosis; (3) kidney of a patient with amyloidosis of parenchymal organs (liver, spleen, kidney) obtained 3 hr. post-mortem.

The tissues were immediately cut into specimens about 1 mm.^{3} and were fixed in both Dalton's solution



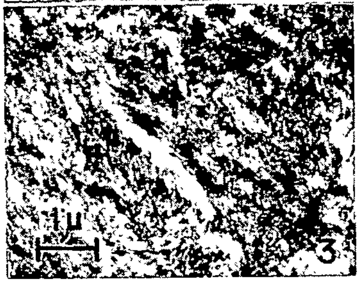


Fig. 1. Portion of rabbit glomerulus demonstrating amyloid fibrils in haphazard pattern. *A*, Amyloid; *End*, glomerular endothelial cytoplasm. (× *c*. 17,500)

Fig. 2. Portion of subcutaneous tissue biopsy of patient with primary systemic amyloidosis. Amyloid fibrils arranged in curved bundles. (× *c*. 23,500)

Fig. 3. Portion of renal tubular interstitial area of kidney obtained 3 hr. post-mortem. Fibrils in amyloid in swirls. (× 8,000)

and buffered osmium tetroxide in sucrose, then dehydrated in alcohol. Alternate specimens were put through 1 per cent phosphotungstic acid in absolute alcohol. The tissue was embedded in *n*-butyl methacrylate, and polymerized overnight with benzoyl peroxide at 60° C. Thin sections 250–500 A. thick were cut on a Porter–Blum microtome and examined in an *RCA-EMU-2B* electron microscope. Successive thick sections (up to 0·5μ thick) were cut from the same blocks and studied with the phase microscope; and, after staining, with the light microscope in order to determine the exact location of the amyloid. Formalin-fixed sections of the same material which had been prepared simultaneously with the osmium fixation were also cut, stained with hæmatoxylin and eosin, crystal violet, congo red and van Gieson dyes, to permit estimation of the amount of amyloid present. All three types of amyloid-containing tissues studied, bound congo red and exhibited metachromasia with crystal violet.

In the rabbit kidneys, the appearance of the amyloid was striking. It was localized between the basement membrane and the endothelial cell cytoplasm and in specimens fixed without phosphotungstic acid, had a fine granular appearance with delicate filaments running through it. In the material stained with phosphotungstic acid the filaments were more clearly defined and in several areas there was a suggestion of beading along the strands. The distribution of the filaments was either haphazard (Fig. 1) or, in areas near endothelial cell cytoplasm, in bundles. Although limitations imposed by sectioning prevented the precise delineation of fibril dimensions, they appeared to range in length from 1200 to 5000 A., and in width from 50 to 120 A.

The biopsy specimen of the patient with extensive primary amyloidosis also showed wavy bundles of delicate fibrils in the electron microscope. These correlated with the areas of amyloid as seen in the phase microscope and in stained sections. The dimensions were similar to those seen in the rabbit amyloid. The width varied from 70 to 140 A. and long strands up to 16,000 A. were measured. No cross-banding was apparent. These fibrils were often seen near collagen fibrils in the same section but were easily distinguished from them since the latter had a greater width and characteristic cross-banding. Fig. 2 demonstrates the delicate, wavy nature of the amyloid filaments as seen at a magnification of *c*. 23,500.

The amyloid in the kidney of the patient with parenchymatous involvement also demonstrated fine bundles of filaments similar to those noted above. Fig. 3 represents a 8,000-magnification of an area of amyloid in the renal interstitial area. The fine curved nature of the fibrils is again apparent.

Thus amyloid of diverse origin had similar submicroscopic structural characteristics. The fibrils as observed thus far appear to be morphologically distinct from collagen, thus corroborating previous chemical studies[3]. Further isolation and characterization studies of this fibrous element should contribute to our understanding of amyloid.

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Relationship between Salinity and Breeding of *Anopheles gambiae* in North-Eastern Tanganyika

A FEATURE of interest in the transmission of malaria in the Pare area of Tanganyika, before residual spraying, was the low sporozoite rate in *A. gambiae*, infections of less than 1 per cent normally occurring. Two factors thought to contribute to the low sporozoite-rate were facultative feeding on cattle, and a low survival-rate in the vector[1,2]. A further possibility, that could not be excluded, was that the local strain of *A. gambiae* was also relatively resistant to infection or exhibited some innate difference in behaviour that reduced its chance of acquiring an infection, compared with strains in other areas. The existence of a low sporozoite-rate in salt-water *A. gambiae* on the humid coast of Tanganyika[3] gave rise to speculation as to whether the presence of saline soils in the Pare area was not associated there also with the low sporozoite-rate.

In the vicinity of rivers that descend from the South Pare Mountains, there are porous alluvial fans that are not saline. Surrounding these fans are much older impermeable soils from which rainfall and seepages from the mountains evaporate to a much greater extent, and are therefore saline. Salinification of the soils is particularly marked along the edges of fans where river seepages are held up by impermeable soils. 17 soil samples were obtained from different points along the valley between the South Pare and Usambara Mountains. The salinity of each sample was indicated by its conductivity in a 1–5 soil/water suspension at 25° C., and the results expressed as micromhos/cm. Conductivity of soil was 200 by a river, 950 to more than 3,000 in the swamp area, and more than 3,000 micromhos/cm. at the edge of an alluvial fan.

The chloride content of water in which *A. gambiae* was found breeding was estimated by the method of Sinton and Kehar[4], and the results expressed as parts of chloride per 100,000 of solution and as per cent sea-water chloride. Among 42 samples, the parts of chloride varied from 2·5 to 170 or, in terms of chloride concentration in sea water, a range of 0·13 per cent to 8·95 per cent. The distribution of saline breeding places coincided with that of saline soils. Parts of chloride were 2·5–5 near a river, 2·5–55 in the swamp area, and 20–170 at the edge of an alluvial fan.

Recently hatched larvæ from the eggs of 7 *A. gambiae* from huts, and 11 from outdoor box shelters, were subjected to Ribband's test[3] and none survived. Observations were then made, at 30-min. intervals for 8 hr., on mortality of recently hatched larvæ in a series of saline concentrations. The results (Table 1) show that the larvæ survived chloride concentrations equal to 30 per cent sea water for 8 hr., but died within 7½ hr. at 34 per cent.

Table 1. MORTALITY OF *A. gambiae* LARVÆ IN A RANGE OF SALINITIES

Parts Cl/100,000	1,450	1,050	850	800	650	550	525	500
Sea water (per cent)	77	55	45	42	34	30	28	26
Survival (hr.)	0·5	1·0	2·5	3·5	7·5	8·0	8·0	8·0

Ribbands[5] found that *A. melas* on the west coast could develop in 150 per cent sea water, whereas the maximum concentration in which freshwater *A. gambiae* underwent complete development was 37½ per cent sea water. Muirhead-Thomson[3] found evidence that salt-water *gambiae* at Dar es Salaam would not survive salinities higher than 83 per cent sea water, although they survived Ribbands's test. *A. gambiae* from Pare did not survive Ribbands's test or salinities higher than 34 per cent sea water. It is concluded that *A. gambiae* in the Pare area is typical freshwater *gambiae*, and that resemblances in sporozoite rate between *A. gambiae* in Pare, and salt-water *A. gambiae* on the east coast, are not related to the occurrence of saline soils in the former area.

We acknowledge with grateful thanks the help given us by Dr. T. E. Fletcher in providing apparatus and reagents for chloride estimations. We also owe thanks to Dr. D. Bagster Wilson for helpful criticism.

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Relationship between Epiphytic Algal Species and their Macrophytic Hosts

EPIPHYTES on the submerged parts of macrophytes have long been studied, but mainly from the taxonomic point of view. Little is known about the relationship of epiphytes with their host plants, or more particularly, whether certain species of algal epiphytes are associated with certain species of macrophytes. From observations made in Scotland, Sudan and in Malaya, I think that there is possibly some association. Mention was made of this in 1955[1], but since then there seems to have been no published information concerning this aspect of algal ecology.

Field observations are often marred by the fact that it is difficult to separate the effect due to decay from the natural epiphytic flora on healthy growing parts. The answer to such problems is to use healthy plants completely free from epiphytes, and to watch what develops on them in a particular environment. The difficulties in getting such 'clean' plants are innumerable. Dissected growing points are very slow to develop, while seeds of aquatic plants are often difficult to germinate. The use of algicides, such as copper sulphate and potassium permanganate, may not suppress fungi as well unless used in such quantities as may damage the growing points of the macrophytes. A solution to the problem was found by using 'Katadyned' water, which contains free silver ions in active form.

The plants chosen, *Enhydrias angustipetala*, *Naias graminea* and *Utricularia* sp., were all plants common in paddy swamps and in the fish ponds at this Station. Young healthy shoots were washed with a jet of water to free them as much as possible from attached algae, and each species was then placed in a large jar of 'Katadyned' water to which had been added some 'Sterasyl' or silver-coated gravel to maintain the content of silver ions in the water. The new young shoots which grew were completely free from epiphytes, and they in their turn were detached and transferred to fresh 'Katadyned' water. In this way healthy 'clean' plants were obtained.

A good length of the younger shoots of each species was transferred to a large fish pond, and sunk by weighting the lower end with a stone. Each plant was protected by a wire cage to exclude macrophyte-eating fish, but not smaller animals such as Crustacea, Rotifera and Protozoa. The pH of the water was 6·9. At the end of a fortnight the plants had increased in size and were coated with epiphytes.

They were carefully lifted, rinsed in water to free them from loose material, and then preserved in 5 per cent formalin.

A quick observation showed that, apart from some loose filaments of *Mougeotia capucina* (Bory) Agardh, the main epiphytic flora consisted of the diatoms *Gomphonema*, possibly *G. gracile* E. and *Eunotia*, probably *E. pectinalis* (Kz) Rbh. var. *elongata* V.H. and also attached plants of an undetermined species of *Oedogonium* (since no reproductive stages). As wide a selection of leaves as possible was taken, avoiding only the very youngest newly opened ones, which were still devoid of epiphytes. Twenty leaves from each species were examined; in the case of *Utricularia* a leaf consisting of several leaflets. The approximate area of each leaf was determined, and a systematic count of the epiphytes made. The results were expressed as density per sq. mm., the diatoms as cells, *Oedogonium* as attached whole plants. As was expected, the older leaves bore the heavier crops of epiphytes.

Table 1. ANALYSIS OF DENSITIES OF *Gomphonema*

	Total	Mean	Variance	
Macrophyte	Σx	$\bar{x}$	σ^2	$\log_e(\sigma^2)$
Utricularia	280·94	14·05	205·0380	5·32301
Naias	40·91	2·05	2·4217	0·88438
Enhydrias	36·60	1·83	2·2520	0·81182

From the results given in Table 1 it seems at first glance that the density of *Gomphonema* is much higher on *Utricularia* than on the other two species of macrophyte. Applying Bartlett's test for χ^2 it can be shown that this difference is significant.

$$\chi^2 = B/C, \text{ where } B = kn.\log_e S^2 - n\Sigma\log_e(\sigma^2)$$

and $C = 1 + (k + 1/3nk)$

Then $\chi^2 = 108{\cdot}718/1{\cdot}023 = 106{\cdot}26$

For 2 degrees of freedom at the 5 per cent level $\chi^2 = 5{\cdot}99$.

The three *Gomphonema* communities cannot be drawn from one and the same population.

Comparing only *Naias* and *Enhydrias* for *Gomphonema* we have $\chi^2 = 0{\cdot}0496$. For one degree of freedom at 5 per cent level $\chi^2 = 3{\cdot}84$. There is therefore no difference between the density of *Gomphonema* on *Naias* and *Enhydrias*.

No *Eunotia* was found on *Utricularia*, so only *Naias* and *Enhydrias* need be compared.

Table 2. ANALYSIS OF DENSITIES OF *Eunotia*

	Total	Mean	Variance	
Macrophyte	Σx	$\bar{x}$	σ^2	$\log_e(\sigma^2)$
Naias	95·37	4·77	147·9761	4·99721
Enhydrias	1·42	0·07	0·0234	−3·75502

$\chi^2 = 135{\cdot}4$. For 1 degree of freedom at 5 per cent $\chi^2 = 3{\cdot}84$. There is therefore a significant difference between the densities of *Eunotia* on *Enhydrias* and *Naias*.

Since no *Oedogonium* was found on *Utricularia* and only one specimen on all the leaves of *Naias* examined, it is obvious that there is a significantly higher population on *Enhydrias*.

The above results suggest therefore that *Enhydrias* favours the growth of *Oedogonium*, *Naias* that of *Eunotia*, while *Utricularia* bears the heaviest density of *Gomphonema*. These experiments were only preliminary and of short duration, and further experiments will be necessary. However, nothing is known about the physiological relationship, if any, between the host plants and the epiphytes, nor is it known what determines which species of epiphyte shall develop. Should the associations prove true, they must play a very important part in the productivity of waters. In the case of algal-feeding fish, such as *Tilapia mossambica*, the epiphytic flora may play a very important part in its diet; since there is evidence concerning the varying digestibility of the different groups of algae, any factor that may determine which species predominate may be of vital importance in the culture of the fish. It would therefore be of great interest to learn if any other similar experiments and observations have been carried out elsewhere.

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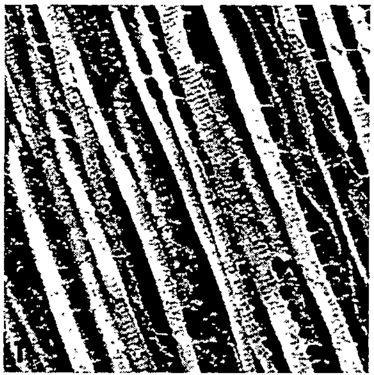
Improved Preservation of Tendon for Electron Microscopy through Wet Freeze-drying

MOST of the information on the fine structure of biological tissues as revealed through electron microscopy has been gained from sections of material fixed with buffered osmium tetroxide, dehydrated in alcohols, and embedded in plastics. The degree of preservation of intracellular detail attained by such handling has been in general very consistent, and the preparatory techniques have been widely accepted as adequate. It has become evident in our recent work that, while some extracellular structures are also regularly well preserved, others seem to suffer considerable damage when processed in like fashion. This has especially been true in the case of tendon, where the component microfibrils appear to become widely separated (Fig. 1). The particular tendons under study are found in the leg of the domestic turkey, and they are of interest to us because they undergo calcification. It is obvious that in order to investigate the relationships between collagen fibrils and mineral crystallites tissue preservation is of the utmost importance.

In our efforts to determine whether or not the structural pattern shown in Fig. 1 represents a true picture of the fibrillar organization of intact tendon, specimens were subjected to different preparatory methods for purposes of comparison. One possibility which was explored arose from a purely physiological observation reported by Mueller and Szent-Györgyi[1]. They noted that when muscle fibres were dehydrated by immersion for three weeks in chilled acetone, transferred to cold ethyl chloride for one week, and then dried in air, they could still be made to contract after rehydration. This suggested that a remarkably high degree of structural preservation must have been attained, and led us to investigate the potentiality of this procedure as applied in histological technique. We have found that when similar treatment with acetone and ethyl chloride is substituted for the osmium tetroxide fixation and alcoholic dehydration steps or for the fixation step alone, sections from methacrylate-embedded tendon fibres present a quite different appearance under the electron microscope (Fig. 2). The collagen microfibrils are in close contact and form wide bands with a definite alignment of the 640 A. striations. The sheet-like configuration resembles that seen in preparations of both teased native collagen fibrils[2] and reconstituted collagen[3].



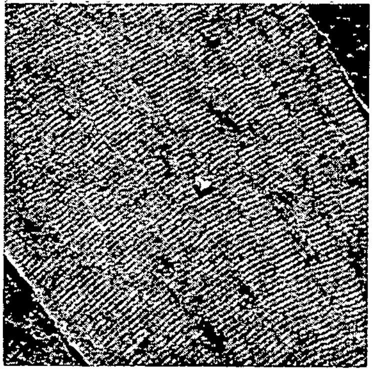


Fig. 1 (top). A thin section of uncalcified tendon from the leg of an 8-week old turkey; fixed in buffered 1 per cent osmium tetroxide, dehydrated in alcohol, embedded in methacrylate

Fig. 2 (below). A thin section of similar tendon which was simply treated with chilled acetone and ethyl chloride before embedding in methacrylate (both *c.* × 11,670)

We believe that this microscopic picture reflects a more intact state of tissue preservation, and more nearly represents the true structure of tendon fibrils than has hitherto been observed in sectioned material.

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BACTERIOLOGY

Bacterial Action in Pond-stored Logs

Extreme porosity was found in sapwood lumber produced from logs of *Pinus ponderosa* and *P. lambertiana* which had been stored in a pond from one to several months. The extreme porosity resulted in substantial over-absorption of water-repellent preservative solutions which are normally applied to millwork, with consequent difficulties in painting and utilization.

Investigation showed that bacteria operating under anaerobic conditions rapidly increased the permeability of the sapwood without substantially affecting strength. The attack was characterized by: (1) removal of parenchyma ray cell contents; (2) corrosion and eventual destruction of parenchyma, particularly in ray tissue. With the assistance of Dr. E. McCoy of the University of Wisconsin, at least one group of the destructive bacteria was identified as *Aerobacillus polymyxa* (flax retting bacteria) and related species. Unidentified bacteria in pond-stored logs have been previously reported by Stutz and Stout (Western Pine Association)[1] in connexion with brown-stain development in pine.

Many bactericidal and related treatments were applied to pond water. In preliminary laboratory tests the most economic and practicable controls found to date are acidification of infected water with sulphuric acid or application of sodium chloride.

Subsequent surveys indicate that this attack is widespread, at least in mill-ponds in California, but not generally recognized. There were some indications that causative bacteria may be present in sound logs before entry into the storage pond but attack was only found in ponded logs.

This work will be reported in detail in the *Journal of the Forest Products Research Society*.

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Cell-Wall Composition of *Leptotrichia* spp.

The status of the genus *Leptotrichia* has long been a matter of controversy, and in the current edition of Bergey's "Manual"[1] it is omitted completely. Nevertheless, there is no doubt of the existence in the oral flora of micro-organisms corresponding to the descriptions of *Leptotrichia*, and entirely distinct from other genera to which they have at various times been relegated by systematists. Two types are commonly found in the mouth, to both of which the name *L. buccalis* has been applied; these were distinguished by us as two species, *L. buccalis* and *L. dentium*[2]. Both are relatively large, filamentous, Gram-positive bacteria, but they differ considerably in morphology and metabolic characters, and the salient question arising from their recognition and distinction is whether they are sufficiently alike to be retained even in the same genus.

To the solution of this problem we have applied the technique of cell-wall analysis, according to the methods of Cummins and Harris[3], with certain modifications.

Sugars and amino-sugars were obtained from whole-cell hydrolysates, and analysed by descending, one-dimensional paper chromatograms using Whatman No. 1 paper and either *iso*propanol (160)/water (40) or phenol (80)/water (20) as solvents. Amino-acids were obtained from cell-wall fractions of cells broken by ultrasonic vibration, and chromatographed as for sugars, using *iso*propanol (70)/water (20)/acetic acid (10), or phenol (80)/water (20) + ammonia.

Leptotrichia buccalis and *L. dentium* yield exactly identical cell-wall amino-acid patterns, consisting of alanine, glutamic acid and DL- or DD-diaminopimelic acid as major components, and traces of glycine, serine, lysine and leucine. From our own comparative studies and the results of Cummins and Harris[4] this pattern appears to be representative of the genera *Nocardia*, *Mycobacterium* and *Corynebacterium*.

Sugar analyses showed arabinose and glucose as the major components of *L. dentium*, but only glucose in *L. buccalis*. Both gave small amounts of hexosamine (probably glucosamine) and ribose. The characteristic sugars of *Nocardia, Mycobacterium* and *Corynebacterium* are arabinose and galactose, which distinguish *L. dentium* from these genera. *L. buccalis* is even more clearly differentiated by its lack of arabinose.

From the evidence so far available it thus appears that the two species described by us[2] may reasonably be retained in the same genus, although it must be recognized that the taxonomic significance of amino-acid and sugar patterns in bacterial cell walls is yet poorly understood. There is already considerable variation in the literature regarding the taxonomic levels, that is, species, genera, etc., at which these patterns function as diagnostic characters. For this reason, the question of relationships between *Leptotrichia* and other groups still cannot be answered with any confidence. On the basis of morphology and cell-wall patterns, relationship to the *Nocardia, Mycobacterium, Corynebacterium* group of genera seems reasonable, whereas upon metabolic characters and cell-wall pattern, relationship with *Lactobacillus plantarum* is possible ; it may be that this apparent divergence in relationships will be reconciled by future work. No relationship to *Fusobacterium* or *Actinomyces* is indicated by our studies of cell walls in these genera.

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Synthesis of Deoxyribonucleic Acid during the Division Cycle of Bacteria

In bacterial cultures undergoing synchronous growth, deoxyribonucleic acid has repeatedly been shown to be synthesized during part of the division cycle only (see review by Campbell, ref. 1). This could, however, be due to the physical or chemical operations used to induce synchronous division and need not reflect the normal pattern of synthesis of deoxyribonucleic acid. We have tested this possibility by examining autoradiograms of cells from uninfluenced cultures growing exponentially which had been exposed to thymidine labelled with tritium for short periods. Tritiated thymidine has already proved useful in studies of the mechanism of replication of deoxyribonucleic acid in bacteria[2]. The present experiments indicate that during normal exponential growth, synthesis of deoxyribonucleic acid is virtually continuous.

Two strains of *Escherichia coli* requiring thymine, namely, $15T^-$ (from the laboratory of Dr. S. S. Cohen) and *B*3 (from Dr. S. Brenner), were employed. These strains differ in morphology, mobility, rates of growth and sensitivity to penicillin. In addition, a wild-type strain of *Salmonella typhimurium* was used. Table 1 lists the media employed and the rates of growth obtained at 37° C. Tritiated thymidine (Schwarz Laboratories, Inc.) with a specific activity of 360 mc./m*M* was added to these media to a concentration of 3–5 μgm./ml. for *E. coli* and 12 μgm./ml. for *S. typhimurium*. Before addition of the labelled compound, exponential growth had been maintained at a constant rate for several generations in the presence of 0·5–1·0 μgm./ml. of unlabelled thymidine. Samples were removed at different times, treated with cold 0·5 *N* perchloric acid for 30 min., washed and resuspended in saline. This suspension was placed on agar blocks and, after the liquid had been completely imbibed, impression smears were made by touching the surface with 'subbed' glass slides (Ilford, Ltd.). The slides were covered with stripping film (autoradiographic film, *AR* 10, Kodak, Ltd.) according to the technique of Doniach and Pelc[3]. The time of contact with the film was selected to give an average of 3–5 grains per bacterium, and after development the bacteria were stained—through the film—with crystal violet.

Control experiments showed that the number of grains produced by the bacteria was reduced to the background value (about 1 grain/$100\mu^2$) after treatment with 100 μgm./ml. deoxyribonuclease for 30 min. at 37° C. Treatment with 0·5 *N* perchloric acid at 70° C. for 20 min. reduced the number of grains by 80–90 per cent, whereas the routine treatment with cold perchloric acid had no demonstrable effect. We therefore assume that nearly all the radioactivity which remains in the cells after extraction with cold acid resides in the deoxyribonucleic acid. Possible deoxyribonucleic acid-precursors of high molecular weight cannot be taken into consideration, since no chemical or genetic test has yet been developed which would distinguish such entities from deoxyribonucleic acid proper.

Table 1 summarizes nine experiments designed to show whether, during a fraction of the average generation time (see column 4), all or only part of the cells of a growing culture incorporate thymidine into their deoxyribonucleic acid. For each experiment the distribution of grains per cell was fitted to a Poisson distribution with the same mean value. This preliminary analysis revealed no systematic deviation from the Poisson distribution (see the *P* values of the last column), and it may therefore be

Table 1

Organism	Culture medium	Average generation time (min.)	Incorporation time as fraction of the average generation time	No. of cells counted	Average No. of grains per cell	Fraction of cells with zero grains	*P* per cent (of fit to Poisson distribution)
E. coli $15\ T^-$	Glucose–salts–thymidine	45	0·1	301	3·36	0·047	20–30
E. coli $15\ T^-$	Glucose–salts–thymidine	45	0·2	240	2·65	0·083	80–90
E. coli *B* 3	Glucose–salts–thymidine	48	0·1	257	2·58	0·112	5–10
E. coli *B* 3	Glucose–salts–thymidine	48	0·2	300	3·27	0·083	0·1–1
E. coli $15\ T^-$	Casamino acids–salts–thymidine	28	0·2	292	3·52	0·058	0·1–1
E. coli $15\ T^-$	Rhamnose–salts–thymidine	64	0·1	283	3·03	0·060	5–10
E. coli $15\ T^-$	Rhamnose–salts–thymidine	64	0·2	140	4·87	0·007	60–70
S. typhimurium	Glucose–salts–thymidine	50	0·2	203	3·29	0·044	80–90
S. typhimurium	Glucose–salts–thymidine	50	0·2	213	4·05	0·009	60–70

concluded that roughly equal amounts of tritiated thymidine are taken up by individual cells during a short period of exposure.

A detailed analysis, to be published elsewhere, has led us to the conclusion that synthesis of deoxyribonucleic acid takes place over more than 80 per cent of the division cycle; it was not possible to decide whether the rate of synthesis remains constant or increases during the cycle. The model on which the analysis was based allows for the fact that some of the cells divide during the period of incorporation of labelled thymidine, and it could be shown that such sources of error as trackiness in the autoradiograms and variation in the individual generation times do not invalidate the interpretation.

Our results indicate that the pattern of synthesis of deoxyribonucleic acid found in synchronous growth experiments is artificial, and great caution must therefore be exerted in interpreting data from such experiments in terms of the normal division cycle. The rapidly growing bacterial cells apparently differ, with respect to their synthesis of deoxyribonucleic acid, from animal and plant cells, where this process seems to be restricted to part of the interphase period.

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Adaptation of Marine Bacteria to Growth in Media lacking Sodium Chloride

THE adaptation of marine bacteria to the ability to grow on ordinary nutrient media prepared with distilled water instead of sea water has been observed in stock cultures; but, paradoxically, procedures designed to acclimatize these forms have not been successful[1,2]. The techniques previously reported have involved successive cultivation of the organisms in media progressively diluted with distilled water. A possible reason for the failure of these trials seems to be the complex nature of the adaptive changes required to allow for the simultaneous reduction or omission of all the components of sea water. Accordingly, the possibility of adapting marine bacteria to growing on media prepared with a synthetic sea water lacking only sodium chloride has been tested.

The cultures employed were isolated from samples of water from the Atlantic Ocean (St. Augustine, Florida) and the Gulf of Mexico (Cedar Key, Florida). All cultures required media prepared with sea water, and their cells lysed when suspended in distilled water. None of the organisms grew in media prepared with synthetic sea water from which sodium chloride was omitted; but on the other hand, sodium chloride alone failed to satisfy their mineral requirements. The synthetic sea water employed was compounded as follows: sodium chloride, 2·4 per cent; hydrated magnesium chloride, 0·53 per cent; hydrated magnesium sulphate, 0·70 per cent; potassium chloride, 0·07 per cent. The organisms grew adequately in media prepared with this salt mixture. The nutrient base in all media was 'Trypticase' (B.B.L.) 1·0 per cent, supplemented with 1·0 per cent fresh yeast infusion (10 per cent yeast). Media from which sodium chloride was omitted contained no added sodium ions, contained less chloride ions and had a lower tonicity; consequently even this single omission posed a complex problem in adaptation.

A number of attempts to adapt these marine cultures to non-dependence on sodium chloride by the dilution of growing cultures failed. These efforts were arranged to permit the optimum opportunity for the induction of the entire population to non-dependence on sodium chloride similar to the reported behaviour of *Escherichia coli* toward increased concentration of sodium chloride[3]. On the other hand, when heavy suspensions of the cultures were plated on the nutrient media prepared with artificial sea water from which sodium chloride had been omitted, a small proportion of the cells grew and produced colonies. These were capable of growing in subsequent culture in the absence of sodium chloride. When similar aliquots were plated on nutrient media prepared with fresh water, no colonies were obtained from any of the cultures tested. The frequency with which the cells independent of sodium ions occurred was compatible with their resulting from mutational events (Table 1). From each of the cultures a representative adapted colony was selected, purified by streaking and was maintained in stock on the medium free from sodium chloride.

Table 1. INCIDENCE OF SODIUM CHLORIDE-INDEPENDENT CELL IN ORIGINAL CULTURES AND STABILITY OF ADAPTED STRAINS

Culture	Incidence of sodium chloride-independent cells in unadapted cultures*	Percentage of adapted cells reverting after growth in sodium chloride†
I	$1\cdot3 \times 10^{-8}$	68·0
II	$1\cdot2 \times 10^{-8}$	0·0
III	$6\cdot3 \times 10^{-8}$	99·2
IV	$3\cdot4 \times 10^{-10}$	99·6

* Incidence is calculated as the ratio of the viable count obtained on the medium lacking sodium chloride to that obtained on the medium prepared with complete synthetic sea water.
† Values are the percentage of cells not capable of forming colonies in the absence of sodium chloride.

Table 2. OSMOTIC FRAGILITY AND GROWTH IN SODIUM CHLORIDE-FREE MEDIA OF ADAPTED AND UNADAPTED CULTURES

Culture	Per cent lysis in distilled water*		Growth in sodium chloride-free medium†	
	Unadapted	Adapted	Unadapted	Adapted
I	79	22	0·04	0·31
II	50	12	0·02	0·35
III	57	29	0·02	0·30
IV	56	28	0·01	0·35

* Per cent lysis is the percentage reduction in optical density resulting when a standardized heavy suspension in sea water is diluted 100 times in distilled water. The standard of comparison is a similar dilution in sea water.
† The values recorded are optical densities of the cultures after 24-hr. growth.
Optical densities were measured by means of a Bausch and Lomb 'Spectronic' 20.

The adapted strains were osmotically less fragile than were the original cultures, although some lysis still occurred when the cells were suspended in distilled water. This residual fragility was not surprising since the medium retained a relatively high salt content despite the omission of sodium chloride. As would be expected, growth in media lacking sodium chloride was better with the adapted forms (Table 2). All the adapted strains were able to grow in media prepared with distilled water, although the initial colonies had apparently been unable to develop in such media. Thus it appeared that strains which had grown in the absence of sodium chloride had developed the additional capacity of growing in media prepared with distilled water. All the strains when grown in such media produced green or blue-green water-soluble pigments.

If the adaptation to non-dependence on sodium chloride in these isolates resulted from the selection of mutants, then logically the adapted character should be retained after being grown in the presence of sodium chloride. Accordingly, the adapted cells were grown in media prepared with sea water and were then tested for reversion. All but one of the cultures indicated some degree of reversion to the wild form, and in two cases it was quite marked (Table 1). This was reflected in the osmotic and growth properties of the cultures as well as a reduced percentage of cells independent of sodium chloride in the culture. These changes occurred during a single cultivation lasting 12 hr. The terminal cell population was about 10^{10} cells/ml. An obvious difficulty exists in the interpretation of these results, since the inclusion of sodium chloride in the medium was probably as rigorous a selecting force as was its omission.

The observations suggest, although by no means prove, that cultures of marine bacteria contain mutant individuals capable of developing in the absence of sodium chloride. Such cells are not able to initiate growth in the nutrient media prepared with distilled water, but require some other mineral component of sea water. For some reason as yet unexplained, the osmolysis of many marine bacteria usually does not occur in the presence of magnesium ions in the concentrations found in sea water[4] (that is, 0·05 M). As a possibility, it is suggested that such mutants growing in sea water media, although genotypically capable of growing in the absence of sea water, are phenotypically osmotically fragile. For their development in the absence of sodium chloride they must grow in the presence of magnesium ions to permit the initial maintenance of the cells. Once grown, such cells have the ability to develop in media prepared with distilled water. The testing of this hypothesis is planned.

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GENETICS

Homozygosity and *S* Gene Mutation

The S locus governing gametophytic self-incompatibility in plants is particularly suited to mutation studies. Pollen grains having an unmutated allele are unable to grow through a style carrying the same allele. In contrast 'mutant' grains produce pollen-tubes which may overcome the incompatibility barrier. Thus, mutation can be scored simply as seeds produced in normally sterile matings, and then subjected to confirmation by progeny phenotypes. Studies of S locus mutations have been confined to heterozygous plants[2-4] as homozygotes are difficult to obtain in many species. Since pollen S phenotype is a gametophytic character, it has been implied that mutation frequencies of alleles in homozygous plants would simply reflect those of alleles in the corresponding heterozygotes. The present study does not support this postulate.

Five S alleles (S_1, $S_2 \ldots S_5$) in *Petunia inflata* L. were assembled into the corresponding five homozygotes and ten heterozygotes at both $2n$- and $4n$-levels. Homozygotes are obtained readily in this self-incompatible species by self-pollination of young buds prior to S gene action in the style. Results will be reported for the five $2n$ homozygotes and three of the $2n$ heterozygotes—S_1S_2, S_1S_5 and S_3S_4. Two or more plants were used of each genotype, where possible, comprising a total of 16 different plants and their clonal propagants. X-rays were delivered to flowers and buds of pollen-parent plants at 250 kV., commonly with a filter of 1/4 mm. copper and 1 mm. aluminium. Pollinations were made exclusively with unirradiated flowers as females, since appreciable ovular damage occurred in flowers treated pre-meiotically (54 per cent abortion at 500 r., 88 per cent at 1,000 r.). Plants were grown and pollinations entirely made in bee-free control chambers at 22·5° C. Results are summarized as proportions of incompatibly pollinated flowers which produced seed-containing pods. Incompatible matings included both self- (for example, $S_1S_1 \times S_1S_1$) and cross-pollinations (for example, $S_1S_3 \times S_1S_1$).

A most impressive feature of the results was the differential response of homozygous and heterozygous clones (Table 1). Homozygous plants rarely set seed in incompatible matings (about 1 seed per 100,000 viable pollen grains), whether irradiated or untreated. In contrast the heterozygotes produced seed-containing pods in 6·8 per cent of the incompatible matings of untreated males and up to 42·0 per cent of those with X-rayed males (Table 1). No significant differences were observed among genotypes within either group. An average of 5·1 seeds per pod was obtained from the 286 selfed pods on treated and untreated heterozygotes, while compatible crosses on the same plants ranged from 180 to 240 seeds per pod. The proportions of seed-containing pods on heterozygous plants varied greatly depending on the time of treatment (Table 1). However, there was no significant variation with time among X-rayed homozygous flowers (heterogeneity $\chi^2 = 9\cdot 2$, $P = 0\cdot 30$). Meiosis occurred about ten days prior to anthesis (range 9–11 days).

Buds treated after meiosis did not differ significantly from the controls in mutation output, in accord with Lewis's observations[3]. The low S mutability of such post-meiotic buds on heterozygous

Table 1. Percentages of incompatibly pollinated Flowers which produced Seed-containing Pods

	Heterozygotes		Homozygotes	
Days*	Percentage pod set	No. of flowers	Percentage pod set	No. of flowers
Control	6·8	147	0·8	250
≮ 6	6·1	82	1·4	140
7–8	10·7	131	3·2	62
9–10	22·2	265	0·5	211
11–12	32·0	256	0·8	255
13–14	42·0	157	0·8	239
15–16	26·4	140	0·5	200
17–18	10·0	70	1·7	182
19–20	18·2	77	0·0	82
≯ 21	6·4	78	0·0	100

* Number of days from X-irradiation to anthesis.

plants has been interpreted to indicate that S gene action occurred immediately following meiosis[2]. However, this low mutability in post-meiotic haploid cells would be accounted for if a major proportion of S mutation somehow depends on S allelic heterozygosity within the target cell. This sheds doubt on the validity of employing S mutation frequencies (in heterozygotes) to define the time of S gene action. An alternative argument is that S gene action in the pollen occurs as late as the second mitotic division—a timing which could account for the difference in place of inhibition of bi- and tri-nucleate grains[1].

The following mutation frequencies per million viable pollen grains were calculated from the data (11–12 days prior to anthesis is ±pre-meiotic interphase): 9·9, homozygote control; 21·4, homozygote—1,000 r. at 11–12 days; 84·0, heterozygote control; 1,320·0, heterozygote—1,000 r. at 11–12 days.

These values may serve as rough indices of mutation-rates. Variables influencing these calculations include: (*a*) the number of pollen grains, which ranged from 1,800 to 4,500 per pollination for the clones used; (*b*) pollen viability *in vitro*, which dropped to 46 per cent of control-rates in flowers treated between 9 and 16 days with 1,000 r. In addition: (*c*) seed sets averaged 3·0 for control pods, while pods from heterozygotes treated at 9 days or less averaged 3·0 seeds, from 9 to 14 days averaged 5·0 seeds and for greater than 14 days, 6·4 seeds. Finally (*d*) of the 36 'mutant' progeny grown approximately two-thirds have reacted as S mutants.

Twelve of these mutants studied have shown part inactivation of pollen, a phenomenon which led Lewis[3] to postulate that the S locus is bipartite with separable pollen and stylar units. One other mutant plant was of particular interest, for it reacted as if the mutant allele was a cross-over recombinant with the pollen activity of gene S_1 and the stylar activity of allele S_2.

These observations could be interpreted to suggest that the relatively high S mutability of heterozygous cells may occur as a result of genetic interchange. Equal crossing-over or gene conversion would be expected to produce mutants only in S heterozygotes, a significant possibility if the locus is a pseudoallelic aggregate or a composite of separable sub-units. Alternatively, if the S locus comprises synaptically equivalent stylar- and pollen-units, unequal crossing-over could lead to part mutation of pollen in heterozygotes by assembling on the same chromosome two alleles or pollen-units which interact by competition in the pollen (competition interaction leading to full self-fertility occurs in all ten heterogenic pollen classes of tetraploids derived from the heterozygous diploids studied). Unequal crossing-over also would produce partly deficient pollen gametes in both homozygous and heterozygous plants. It is hoped that a detailed investigation of mutant alleles will shed light on the relative significance of these events.

This investigation was conducted at Brookhaven National Laboratory under the auspices of the U.S. Atomic Energy Commission.

J. L. Brewbaker
N. Shapiro

Brookhaven National Laboratory,
Upton, New York, 1.
Jan. 30.

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[1] Brewbaker, J. L., *J. Hered.*, 48, 271 (1957).

[2] Lewis, D., *Heredity*, 3, 339 (1949).

[3] Lewis, D., *Heredity*, 5, 399 (1951).

[4] Pandey, K. K., *Genetics*, 41, 327 (1956).

Possibility of Assortive Mating in the Arctic Skua

Data have recently been collected in Caithness and Shetland on the numbers of the different mating types, dark × dark, dark × pale and pale × pale, of the colour phases of the Arctic skua, *Stercorarius parasiticus*. Although on Fair Isle intermediates, very similar to darks, are recognized; in the remainder of these data, this distinction is not made: for this reason, the intermediates in the Fair Isle data have likewise been added to the darks.

The observations at present available are given in Table 1, together with the date and names of collectors. The Fair Isle data were extracted directly from the record books there.

Table 1

	$D \times D$	$D \times P$	$P \times P$
Fair Isle, 1954–58 (Williamson, K., and Davis, P. E.)	64	34	10
Foula, 1948 (Venables, L. S. V., and Venables, U. M. (ref. 1))	9	7	2
Unst, 1948 (Venables, L. S. V., and Venables, U. M. (ref. 1))	36	15	4
Yell and Fetlar, 1948 (Yeates, G. K. (ref. 2))	36	25	5
Noss, 1946 (Perry, R. (ref. 3))	21	9	7
Caithness, 1953 (Pennie, I. D. (ref. 4))	9	11	1
Totals	175	101	29

D, dark; P, pale

In the Caithness data, the single pale × pale mating was described as a pale × intermediate pair. The description of the intermediate, however, showed that this bird was in fact what would have been called a 'dusky' pale at Fair Isle. This means that the neck and belly are cream rather than white; but these matings have always produced apparently normal pale-phased chicks and are thus included with the pales: what are called 'intermediates' at Fair Isle lack the pale belly.

In the analysis given in Table 2, 2 × 2 contingency tests of independence have been employed: χ^2 for one degree of freedom with Yates's correction has been calculated.

Table 2

Locality	χ^2	Locality	χ^2
Fair Isle	1·99177	Yell and Fetlar	0·0078391
Foula	0·028800	Noss	5·04175
Unst	0·79781	Caithness	0·27320
	Total data	5·34064 (deviation χ^2)	

The χ^2 value calculated for all the data is thus found to be significant at just above the 2 per cent level. It is therefore important to test whether any significant heterogeneity is present. By summing all the separate χ^2 values, χ^2_{total} for 6 degrees of freedom is found to be 8·1412. The heterogeneity χ^2 is now obtained by subtracting $\chi^2_{\text{deviation}}$ from χ^2_{total}. We thus find,

$$\chi^2_{\text{het.}}\ (5 \text{ degrees of freedom}) = 2{\cdot}8005$$

This value clearly does not approach significance.

The conclusion to be reached from these results is that a strong possibility of a departure from random mating among the phases of the Arctic skua exists: a significant excess of like over unlike matings is present, thus indicating a tendency towards homogamous mating.

It is interesting to speculate on the advantages to be gained from this tendency towards homogamy. Fisher[5] says of homogamy in man: "Its principal biometric effects seem to be to increase the genetic variance produced by a given number of Mendelian factors with given gene ratios, and so to increase in a fixed proportion the intensity of the selection to which each is exposed". In this sentence, Fisher is, of course, discussing quantitative variation. It would seem likely, however, that homogamy involving major genes will act in a similar manner by affecting the modifiers of these genes and thus increasing the variability of the expression, especially of the heterozygote. This must lead to a more rapid evolution of dominance: indeed, at Fair Isle, it has been noted that dark appears to be semi-dominant.

Fisher also suggests that the causes of homogamy are scarcely to be distinguished from those which, in sexual preference, produce direct selective effects. Sexual preference might have evolved directly, by the lessening of competition among the more variable families; but there also appears to be the possibility of the evolution of sexual preference by a form of sexual selection. On Darwin's theory of sexual selection in monogamous birds, Fisher[5] says: "He [Darwin] supposes in effect that there is a positive correlation in the females between the earliness with which they are ready to breed, and the numbers of offspring they rear, variations in both these variates being associated, as Darwin suggests, with a higher nutritional condition. Whether this is so in fact it is difficult to say, but it should be noted that the dates of the breeding phenomena of a species could only be stabilized if birds congenitally prone to breed early did not for this reason produce more offspring. The correlation required by Darwin's theory must be due solely to non-hereditary causes, such as chance variations of nutrition might supply. Whether or not there is such a correlation, it would seem no easy matter to demonstrate".

If the sexual preference in question were correlated with early breeding, then clearly the evolution of this preference would prove fairly rapid. On the other hand, if no such correlation were initially present, sexual selection might still result in the enhancement of the sexual preference. The early females must have a wide choice of mates not only in respect of preference for like-phased matings but also for characters like quality of display, physique, or other plumage characteristics. Thus, though it is true that if the proportion of females tending to homogamy is the same in late as in early breeding birds, then the same proportions in the phases of the males will be available to the late as well as the early females: yet, the males left for the late females may be deficient in other respects, thus leaving the late females with a more limited choice of mates; moreover, random fluctuations in the numbers of the different phases must further cut down the choice. This theory demands that there should be congenital variations in the sexual preference in relation to breeding time. It should be noted that in the Arctic skua, birds generally pair for life—divorces are fairly rare—and so this form of selection must be much slower than in a species in which new pairs are formed each year.

P. O'Donald

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Feb. 14.

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[1] Venables, L. S. V., and Venables, U. M., "Birds and Mammals of Shetland" (Edinburgh, 1955).

[2] Yeates, G. K., "Bird Haunts in Northern Britain" (London, 1948).

[3] Perry, R., "Shetland Sanctuary" (London, 1948).

[4] Pennie, I. D., *Brit. Birds*, **46**, 105 (1953).

[5] Fisher, R. A., "The Genetical Theory of Natural Selection", 1st and 2nd edit. (Oxford and New York, 1930 and 1958).

Recoverable Lethal Mutations in *Drosophila* Sperm

In an experiment with fractionated irradiation of *Drosophila melanogaster* males Lüning and Hannerz[1] showed that there was induced the same rate of chromosome breaks at anoxia as in air, but that there was a recovery after irradiation at anoxia which, however, could be blocked by a fraction of irradiation in air. Lüning and Söderström[2] extended these observations to sex-linked recessive lethals and concluded that there existed a similar recovery process among this type of mutations as among chromosome breaks.

Irradiation at anoxia induced changes which could either result in a recessive lethal mutation or reversion to a non-lethal state which could not be distinguished from the original state. If a second fraction of irradiation was given in air within 15 min. after the treatment at anoxia the recovery process was blocked and a rate of recessive lethals was obtained equal that when the whole of the dose was given in air.

In a paper presented to the second Geneva Conference on the Peaceful Uses of Atomic Energy, Lüning showed that the recovery of chromosome breaks could be blocked if the second fraction (in air) was given within 30 min. but not when given on later occasions.

From these results it was concluded that the recovery occurred between 30 and 40 min. after irradiation, and when it had recovered the subsequent irradiation in air had no influence.

A similar analysis using recessive lethals would be of great interest. First, the question arose whether there could be determined a time within which recovery occurred. The establishment of such a borderline should also give a proof of the existence of recoverable mutation processes. Secondly, it was desirable to know whether this borderline agreed with that obtained from chromosome breaks.

In order to study this, the conventional Muller-5 technique was used. 3–4 days old *cv:sc*^{8}*Y* males were given nitrogen for 15 min. before and during the treatment (5 min. = 2,750 r.). The males were then divided into four groups. After varying intervals, they were irradiated in air (3 min. = 1,650 r.). The intervals were chosen to test agreement with the recovery process in chromosome breaks, namely, 15, 30, 40 and 50 min. The males were mated for 6 hr. The females were then allowed to oviposit for two three-day periods. The procedure was then the conventional one. The criterion on lethality has been at least 12 *M5* males but no *cv* males. Some cultures were analysed also in F_3.

Four repeats were made which gave consistent results and for that reason are combined in Table 1.

As is seen from Table 1 the series falls into two groups with the borderline between 30- and 40-min. intervals, which agrees with that from chromosome breaks. Furthermore, the two series with intervals 15 and 30 min. are consistent and significantly higher than the series with 40 and 50 min. interval. This result is in agreement with the expectancy if the

Table 1

Interval	Recessive lethals	Tested X-chromosomes	Recessive lethals (per cent)
15 min.	222	2,154	10·3
30 min.	220	2,026	10·9
40 min.	161	2,049	7·9
50 min.	172	2,192	7·8

recovery of potential recessive lethals occurred between 30 and 40 min. after irradiation at anoxia. The establishment of this borderline may be taken as a proof that there may exist recoverable mutations, although it does not give any information about the ratio of mutations which has this possibility.

K. G. Lüning
H. O. Henriksson
Institute of Genetics,
University of Stockholm. Feb. 11.

[1] Lüning and Hannerz, *Hereditas*, 43, 549 (1957).
[2] Lüning and Söderström, *Hereditas*, 43, 563 (1957).

PSYCHOLOGY

Effects of Independent Variations in Stimulus and Response Probability

The time taken by human beings to react to one of a number of possible signals increases with the number of alternatives involved. The effects of jointly varying stimulus and response uncertainty have been long known and adequately discussed[1,2]. In the present investigation these were varied independently, by using situations where the same response was required for a number of stimuli. The number of responses, and the ratio of response/stimuli were varied.

Card sorting was used as a convenient task for a pilot study. The subject turned and dealt cards from packs held in the non-dominant hand, on to a number of piles. Each pile represented a group of stimuli to which the same response was required. The stimuli were letters and figures (72 point) stencilled on the cards in indian ink. Packs were made up for each condition, so as to vary the number of different symbols for each pile; the number of piles was of course constant for each condition.

Four conditions of response uncertainty were used, four packs for each condition being employed. In one condition packs were to be sorted into two piles, there being one, two, four and eight symbols per pile. Cards were sorted into letters, or figures.

The other conditions used four, six and eight piles, with response/stimulus ratios of 1/1, 1/2, 1/3 and 1/4 in each case. Ten subjects were tested on condition one, and a fresh batch of twelve on condition two. Four trials were given on each pack (that is, each response/stimulus ratio). A third batch of nine subjects was used on the six- and eight-pile conditions. Six of these had eight trials with each pack; the remaining three had sixteen trials with each pack. Sorting time was taken with a stop-watch. Packs were given in random order. For the first sortings in each condition, but never afterwards, indicator cards were attached to the boxes into which the cards had to be sorted. The order of the boxes from left to right was varied randomly for each subject. Subjects were students at a teachers' training college, and female shop assistants. No significant differences appeared between these groups.

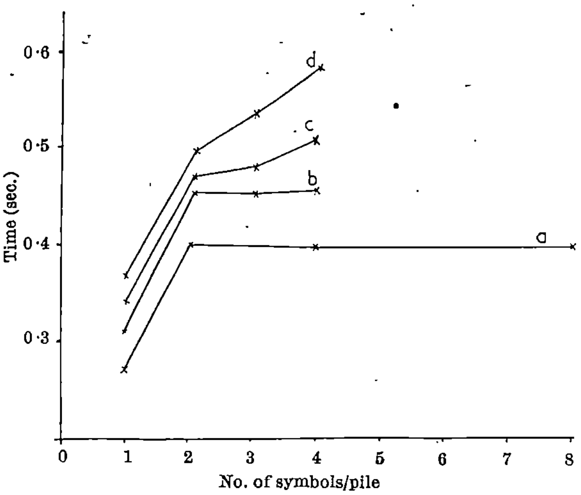

Fig. 1. *a*, 2-pile condition; *b*, 4-pile condition; *c*, 6-pile condition; *d*, 8-pile condition. Decision time/card was obtained by subtracting mean movement time, obtained individually for each subject, from the mean sorting time for each condition

The results of these tests are shown below. In condition one there was a marked significant increase in time between pack I and pack II. Times for packs II, III and IV did not differ. In condition two the results were similar. In condition three the most striking difference remains that between packs I and II. There is a non-significant difference between packs II and III, and a significant ($P < 0{\cdot}02$) increase between pack III and pack IV. In the fourth condition there are highly significant differences between all packs. The most striking is that between pack I and pack II. The results of the three practised subjects on the last conditions were of the same pattern.

In the last three conditions digits had been sorted into two of the piles. It was felt that the results might have been partly explained by the diminishing effect of the figures/letters dichotomy as the number of piles increased. Accordingly, the two- and four-pile conditions were repeated on six subjects practised in earlier trials using letters only. After eight trials on each pack in both conditions, the results showed the same pattern as the earlier tests. The increased practice necessary suggests that the figure/letter dichotomy had been used by the subject in earlier tests.

The results were still open to the interpretation that, despite the precaution of giving packs to the subjects face down, a small increase in reaction time with increase of stimuli/response was masked by subjects 'taking up the slack', and overlapping movement and decision-time to some extent. A choice reaction-time apparatus was used for investigating this, push buttons representing piles, and stimuli being projected on to a screen before the subject. Individual reaction-times were measured with a 'Dekatron' timer. Six subjects were used on the two-pile condition (letters/figures) and four on a four-pile condition (2 letters/figures, 2 letters only). The results gave the same pattern as the card sorting tests. In the four-pile condition considerable practice was necessary (500 presentations for each response/stimulus ratio) before this pattern emerged.

These results suggest that there are certain limits within which the response-time to groups of stimuli is dependent on the number of possible responses, rather than on the number of different alternative stimuli to which each response is to be made.

This work was carried out under a Department of Scientific and Industrial Research studentship, and the supervision of Mr. D. E. Broadbent.

P. M. A. Rabbitt
Psychological Laboratory,
University of Cambridge. Feb. 3.

[1] Quastler, H., "Information Theory in Psychology" (Illinois, 1955).
[2] Hick, W. E., *Quart. J. Exp. Psychol.*, 4, 11 (1952).

FORTHCOMING EVENTS

*(Meetings marked with an asterisk * are open to the public)*

## Monday, April 27

Institute of Actuaries (in Staple Inn Hall, High Holborn, London, W.C.1), at 5 p.m.—Mr. S. Benjamin: "The Theory of Games and Its Application to the Rate of Interest".

Royal Geographical Society (at 1 Kensington Gore, S.W.7), at 5 p.m.—Mr. E. M. Yates: "Dating the Cultural Landscape, with Examples Drawn from West Sussex".

Institution of Electrical Engineers, Radio and Telecommunication Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. G. F. Swann: "The Field Strengths Required for the Reception of Television in Bands I, III, IV and V".

University College (in the Anatomy Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. O. Heckmann (Hamburg Observatory): "Newtonian Cosmology".*

University of London (at Bedford College, Regent's Park, London, N.W.1), at 5.30 p.m.—Prof. J. Hämmerling (Max-Planck-Institut für Meeresbiologie, Wilhelmshaven): "Some Problems of Cell-Physiology with special reference to Studies on Acetabularia".* (Further lectures on April 28 and 29.)

Royal Aeronautical Society (at the Institution of Civil Engineers, Great George Street, London, S.W.1), at 6 p.m.—Lecture on "The Electronics of Guided Missiles".

Royal Society of Arts (at John Adam Street, Adelphi, London, W.C.2), at 6 p.m.—Prof. J. J. Vincent: "Research in Cotton". (Second of three Cantor Lectures. Further lecture on May 4.)

Monday, April 27—Thursday, April 30

Corrosion Exhibition (at the Horticultural Hall, Westminster, London, S.W.1).*

Tuesday, April 28

Institution of Chemical Engineers (at the Park Lane Hotel, Piccadilly, London, W.1) at 10.45 a.m.—Annual General Meeting.

University of London (in the Large Lecture Theatre, Royal College of Science, Imperial Institute Road, London, S.W.7), at 5.30 p.m.—Prof. W. Lochte-Holtgreven (University of Kiel): "Light Emission Associated with Formation of Negative Ions". (First of three lectures on "Spectroscopic and Magnetic Studies of Thermally Excited Plasmas". Further lectures on May 1 and 4.)*

Institution of Mechanical Engineers, Education Group (at 1 Birdcage Walk, Westminster, London, S.W.1), at 6 p.m.—Discussion on "Extended University Courses for the Better Graduate".

Society of Instrument Technology (at Manson House, Portland Place, London, W.1), at 6 p.m.—Mr. M. E. F. Howarth and Mr. B. P. Watt: "Measurements in the Photographic Industry".

British Institution of Radio Engineers, Medical Electronics Group (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m. Prof. G. Causey and Mr. R. S. Page: Two papers on "Electron Microphony".

Society for Analytical Chemistry, Physical Methods Group (at the Brunel College of Technology, Woodlands Avenue, Acton, London, W.3), from 6.30 p.m. to 9 p.m.—Demonstration of Laboratory-Made Equipment.

Wednesday, April 29

Geological Society of London (at Burlington House, Piccadilly, London, W.1), at 3 p.m.—Annual General Meeting. Dr. C. J. Stubblefield, F.R.S.: "Evolution in Trilobites" (Presidential Address).

University College (in the Anatomy Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. O. Heckmann (Hamburg Observatory): "Some New Aspects of Relativistic Cosmology".*

Challenger Society (at the Linnean Society, Burlington House, Piccadilly, London, W.1), at 5.45 p.m.—Annual General Meeting, followed by Dr. G. S. Carter: "The Conditions of Evolution in the Deep Seas".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Mr. G. de Q. Robin: "Antarctic".

Wednesday, April 29—Thursday, April 30

Institution of Electrical Engineers (in conjunction with the British Nuclear Energy Conference, at Savoy Place, London, W.C.2.—Convention on "Thermonuclear Processes".

Thursday, April 30

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. R. L. F. Boyd and Mr. N. D. Twiddy: "Electron Energy Distributions in Plasmas"; Mr. R. L. F. Boyd and Mr. J. B. Thompson: "The Operation of Langmuir Probes in Electro-Negative Plasmas".

Institute of Information Scientists (at the Berners Hotel, 10 Berners Street, London, W.1), at 6 p.m.—Symposium on "The Adaptability of Experience—an Inquiry into the Subject Qualifications Needed for Information Work". Chairman: Mr. L. J. H. Haylor. Speakers: Miss I. M. Slade, Mr. A. Gordon Foster, Mr. C. W. Hanson and Mr. F. Newby.

Institution of Electronics (in the Assembly Hall of the University of London Institute of Education, Malet Street, London, W.C.1), at 7 p.m.—Mr. G. H. Byford: "Measurements in Aviation Physiology".

University of London (at the Swanley Hall, Withersdane, Wye College, near Ashford, Kent), at 8.15 p.m.—Dr. I. A. Galloway: "Recent Advances in the Study and Control of Animal Virus Diseases".*

Friday, May 1

British Psychological Society, Occupational Psychology Section (in the Department of Psychology, Birkbeck College, Malet Street, London, W.C.1), at 1 p.m.—Mr. John Annett: "Problems of Training".

Antiquarian Horological Society (at the Science Museum, London, S.W.7), at 7 p.m.—Annual General Meeting.

Saturday, May 2

Association of Agriculture (at Senate House, University of London, W.C.1), at 10 a.m.—Conference on "Further Aspects of Animal Physiology".

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Assistant Lecturer (with a degree in botany with some zoology) in Biology—The Registrar, University College of North Staffordshire, Keele, Staffs (April 30).

Assistant Lecturer (preferably with special interests in economic geography and statistics) in the Department of Geography—The Registrar, The University, Leeds (May 1).

Assistant Librarian (Chartered Librarian)—The Establishments Officer, Zoological Society of London, Regent's Park, London, N.W.1 (May 1).

Lecturer (with a good honours degree and preferably special qualifications in servo-mechanisms applied to electrical machines) in Electrical Engineering—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 1).

Assistant Lecturer (with a good honours degree in psychology and preferably some experience of teaching and research) in the Department of Psychology—The Registrar, The University, Leeds 2 (May 2).

Experimental Officer or Assistant Experimental Officer (with analytical experience) in the Technical Chemistry Department, to work on problems connected with grass and milk—The Secretary, The Hannah Dairy Research Institute, Kirkhill, Ayr, Scotland (May 2).

Lecturer in Physics and/or Chemistry—The Principal, Borough Road College, Isleworth, Middlesex (May 4).

Senior Scientific Officer (with a science degree of a university in the United Kingdom with passes in biochemistry, zoology, botany, etc., and preferably five-years experience in serology in the Health Service basic grade of Scientific Officer)—The Director, Regional Blood Transfusion Centre, Churchill Hospital, Headington, Oxford (May 2).

Lecturer in Physiology—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 4).

Assistant Lecturer (with a good honours degree in zoology and special interests in parasitic protozoa) in Zoology—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 5).

Lecturer in Biochemistry—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 7).

Lecturer (with a good honours degree and preferably a special interest in the field of numerical analysis) in Applied Mathematics—The Registrar, King's College (University of London), Strand, London, W.C.2 (May 7).

Assistant Lecturer (preferably with a special interest in systematic botany) in Botany, and a Tutorial Assistant in Geology—The Registrar, University College of Wales, Aberystwyth (May 8).

Lecturer or an Assistant in the Department of Mathematics—The Secretary, The University, Aberdeen (May 9).

Lecturer or Assistant Lecturer (Veterinary Surgeon) in Veterinary Pathology—The Secretary, Royal Veterinary College (University of London), Royal College Street, London, N.W.1 (May 9).

Research Fellow in the Department of Chemistry, for work on heterogeneous catalysis—Prof. C. Kemball, The Queen's University, Belfast (May 9).

Senior Lecturers (with a good university degree in requisite subject, considerable postgraduate experience in research and/or teaching, and conversant with tropical work in the appropriate subject) in *(a)* Horticulture, *(b)* Animal Husbandry and *(c)* Poultry Husbandry at Kumasi College of Technology—The Council for Overseas Colleges, 12 Lincoln's Inn Fields, London, W.C.2 (May 11).

Lecturer in Education, and Assistant Lecturers in Biochemistry and Physiology—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (May 14).

Research Demonstrators in Physics, Zoology, Geology and Mining; and a Research Assistant in Engineering—The Registrar, University College of South Wales and Monmouthshire, Cathays Park, Cardiff (May 14).

Lecturer (preferably with qualifications in the comparative physiology of invertebrates), and an Assistant in the Natural History Department—The Secretary, The University, Aberdeen (May 15).

Research Assistant (Physical Chemist), for work with organometallic compounds—The Secretary, The University, Exeter (May 15).

Research Fellows (2) in the Department of Medical Chemistry, John Curtin School of Medical Research, Australian National University—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, May 31).

Biochemist, Scientific Officer or Senior Scientific Officer grade (with a first- or second-class honours degree in biochemistry, and preferably postgraduate experience), to work on biological methods of preparing organic compounds labelled with radioactive isotopes—The Personnel Officer, Radiochemical Centre, U.K.A.E.A., Amersham, Bucks.

DEMONSTRATORS, INSTRUCTORS and ASSISTANT PROFESSORS IN THE DEPARTMENT OF PHYSICS, University of British Columbia, Vancouver—Dr. G. M. Shrum, c/o British Columbia House, 1–3 Lower Regent Street, London, S.W.1.

LABORATORY TECHNICIAN (with bacteriological or virological experience), for virus research—The Medical Superintendent, Common Cold Research Unit, Harvard Hospital, Salisbury, Wilts.

LECTURER (physicist with experience in X-ray crystallography, a knowledge of electronics and control mechanisms, and preferably previous experience in the rubber field) IN RUBBER PHYSICS—The Clerk to the Governors, National College of Rubber Technology, Northern Polytechnic, Holloway Road, London, N.7.

MASTER TO TEACH MATHEMATICS up to university scholarship standard—The Headmaster, Framlingham College, Framlingham, Suffolk.

MASTER TO TEACH PHYSICS to advanced level—The Headmaster, Malvern College, Worcestershire.

MATHEMATICS TUTOR (honours graduate in mathematics), to prepare to University of London degree standard—The Science Director, University Correspondence College, Burlington House, Cambridge.

RESEARCH PHYSICIST (preferably with experience in the use of ultra-high vacuum systems or in the chemical physics of surfaces) IN THE DEPARTMENT OF PHYSICS, for work which will involve electrical measurements applied to the study of surface contamination processes on semiconductors—The Professor of Physics, University of Reading, Physics Research Laboratories, Upper Redlands Road, Reading.

SCIENTIFIC ASSISTANT (ABSTRACTOR) (with a degree in agriculture or natural science, and a knowledge of languages)—The Director, Commonwealth Bureau of Pastures and Field Crops, Hurley, near Maidenhead, Berkshire.

SCIENTIFIC OFFICER (BOTANIST or AGRONOMIST), to work on the plant species and cultural conditions giving the best yields in the large-scale separation of leaf protein—The Secretary, Rothamsted Experimental Station, Harpenden, Herts.

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(*not included in the monthly Books Supplement*)

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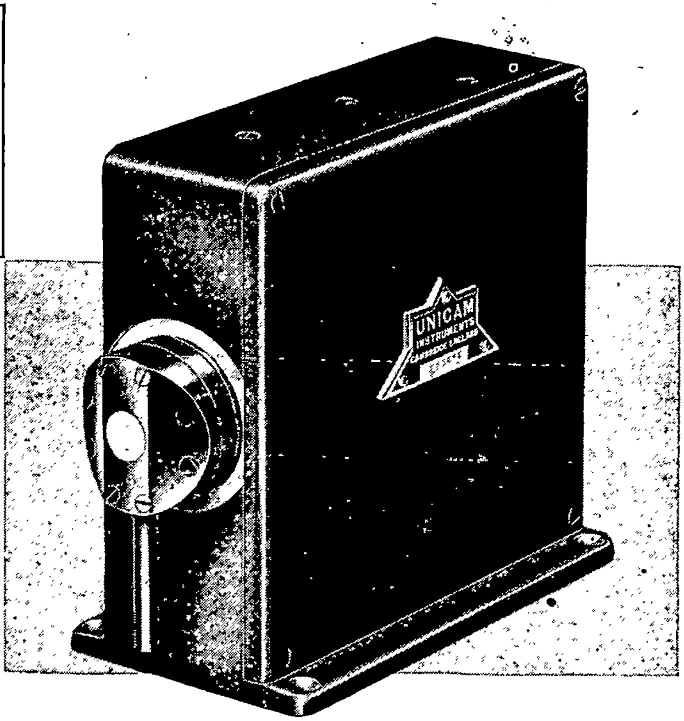

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SCIENCE AND TECHNOLOGY IN THE UNITED STATES

THE appointment of Dr. J. R. Killian as special assistant for science and technology to President Eisenhower and the expansion of the activities of the National Science Foundation which followed swiftly on President Eisenhower's message to Congress of January 27, 1958, have been welcomed as facilitating Anglo-American co-operation and strengthening the organization of the Western world both in science and in defence. The essential ideas for these developments are to be found in reports issued earlier, notably in Dr. Vannevar Bush's report, "Science—the Endless Frontier", and the Steelman report, "Science and Public Policy" in the United States, and in the Barlow report on scientific staff in Great Britain. The United States is now, indeed, giving effect to ideas which in Great Britain have found expression in the establishment of the Advisory Council on Scientific Policy and the Defence Research Policy Committee, for example.

The address on "Science and Public Policy" which Dr. Killian delivered on December 25 to the American Association for the Advancement of Science shows how vigorously the Federal Government is implementing the new policy and how much has already been done to strengthen the position of both science and technology in the United States. This first report of Dr. Killian on the work of his office and of the President's Science Advisory Committee[*] is of great interest to the scientist and technologist in Britain, not only as summarizing what has been done but also from the point of view of eliminating weaknesses in our organization which have become apparent during the past year or so. Reference has indeed already been made in these columns to the report of the Science Advisory Committee's Panel on Scientific Information. This address, and the report of the Committee's Panel on Research Policy, to which Dr. Killian refers in detail, provide ample evidence to justify Dr. Killian's claim that the President's proposals have already been translated into action.

The expansion of the National Science Foundation, the available funds of which have been increased from 50 million dollars in 1958 to 136 million in 1959, may be appropriately left for consideration with the Foundation's latest annual report, merely noting Dr. Killian's view that it is now one of the Government's major means for advancing science and supporting basic research. Next, Dr. Killian notes the creation, under the Department of Defence Reorganization Act, of a new post of Director of Research and Engineering in Defence, and of the Advanced Research Projects Agency, to sponsor long-range research for defence and to undertake projects of common interest to the military Services. The former appointment indicates the importance now attached in the United States to the formulation at a high level of research and development defence policy and to the supervision of an overall programme. Besides this, the National Aeronautics and Space Administration has been created to provide a civilian-directed and civilian-oriented programme of space science and exploration, including research support for military aeronautics and space programmes, with a National Aeronautics and Space Council, advisory to and presided over by the President.

This new pattern of organization of scientific and technological research in the United States and of advisory service to the Government is quite distinct from the structure existing in Great Britain, but there are some similarities. These similarities are perhaps more marked in the work of the Science Advisory Committee and in the recently established Federal Council for Science and Technology, while on the educational side, under the National Defence Education Act, measures have been taken to strengthen science education that are probably more vigorous than those yet adopted in Britain. Likewise, the recent appointment by the State Department of seven scientific attachés suggests that the United States Government is giving more weight to such appointments than the British Government has yet done in spite of the recommendations of the Advisory Council on Scientific Policy.

Dr. Killian emphasizes that neither he, nor the Science Advisory Committee, has any executive responsibilities. Like the Advisory Council on Scientific Policy in Britain, their functions are purely advisory and they do not even share such responsibilities for the decision of policy as fall on the Lord President of the Council. They are charged with providing the best scientific advice and with making recommendations for the advancement of science and technology in the United States, especially by the Federal Government and in matters relating to security and welfare. A principal function is to provide a communications centre for science in the Federal Government, and thus to facilitate intercommunication among various scientific activities within the Government and between the civilian scientific community and the Government.

As in Britain, this is achieved to a considerable extent by the common membership of committees, as well as by the rotation of much of the membership, while the group of panels organized under the Science Advisory Committee enlist the advice and services of a very wide range of experience and knowledge, numbering at present about seventy-five scientists and engineers. Moreover, the Special Assistant for Science and Technology is invited to attend meetings of the National Security Council and the Cabinet, and, when appropriate or requested, to present the views and findings of the Science Advisory Committee. Objective scientific and technological advice can thus be presented effectively at the highest level of government, and it would appear probable that the United States has now a more effective means than Great Britain for ensuring that science and technology play a direct and creative part in formulating public policy. Moreover, particular attention is being given to the problem of placing at the disposal of the Government the creative powers and talent of the younger scientists and technologists, without handicapping either their professional development or their creative work in science and technology.

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[*] A Statement by the President, and Strengthening American Science: a Report of the President's Science Advisory Committee. Pp. iii+36. (Washington, D.C.: Government Printing Office, 1958.) 20 cents.

The principal recommendation in the report, "Strengthening American Science", of the Science Advisory Committee's panel on research policy is the establishment of a Federal Council for Science and Technology to advise the Cabinet on those aspects of the Government's programme which require interdepartmental and Government-wide co-ordination and policy, and which affect science as a whole. The President has already authorized an executive order establishing this Council, and, as recommended by the Committee, membership of the Council will include representatives of the departments and agencies which have substantial research activities, and these representatives will be drawn from the policy-making level. The Committee suggested, for example, that the Council should include the Director of the National Science Foundation, the Commissioner of the Atomic Energy Commission, the Administrator of National Aeronautics and Space Administration and the Director of Defence Research and Engineering; but the Council will be able to call for advice from the Science Advisory Committee, the members of which are largely drawn from outside Government service.

In constitution and membership, the new Council thus appears to be drawn from a higher level than the Council for Scientific and Industrial Research in Britain, and for that reason may well prove a more effective instrument for concerting and co-ordinating Government policy in scientific and technological matters and in all national concerns where such factors are important. The Council is specifically to consider problems and developments in science and technology which affect more than one department or agency, and to recommend policies and other measures to promote the more effective planning and administration of Federal scientific and technical programmes. To that end the Council is to prepare a projection of the programme costs required to meet Federal needs, including both capital and man-power, and to consider the level and type of research financed by the private sector of the economy. It is also to promote effective utilization of Government resources and full co-operation among Government agencies, as well as consider and recommend measures for implementing policy decisions affecting the administration and conduct of Federal programmes in science and technology.

As thus conceived, the new Council, while still advisory, like the Advisory Council for Scientific Policy in Britain, appears to have functions going beyond those of the latter, and much further than those of the Council for Scientific and Industrial Research; and, as already noted, the higher level at which its membership is linked with Government may make it more influential and effective. Much will depend, none the less, on how clearly its advice and recommendations are understood by the Government; but scientists and technologists could scarcely expect their advice to be presented at a higher level. Moreover, the structure proposed appears to be reasonably flexible and to avoid the excessive centralization of authority that can be so inimical to the obtaining and presentation of the best scientific and technical advice.

It remains to be seen how far in practice these new arrangements will solve for the American scientist and technologist the difficult problems of power and responsibility, but they seem to afford reasonable prospect of the scientist and technologist exerting effective influence on public policy. It is not expected that the new Council will solve all the problems in managing research conducted by the Government, but it should assist Government departments in the United States to strengthen their own laboratories and to ensure a fuller and more economic use of their scientific resources. Moreover, the Panel on Research Policy is particularly concerned with the financing and planning of such highly expensive research equipment as particle accelerators in nuclear physics, and the research institutes which are needed or have been proposed in various fields. It recognizes the importance of considering carefully the relation of such institutes to the universities, and the danger of weakening the universities if unsound planning draws away from them too many research workers.

In this connexion, too, the Panel stresses the importance of greater emphasis on basic research. At present about 6 per cent of the U.S. Government's total budget for research and development of more than 5,000 million dollars in 1959 is earmarked for basic research, and the Panel is convinced that more vigorous support of basic research during the past decade would have paid rich dividends in reducing the cost of development. Stress is laid on nurturing new scientific fields and strengthening those, like meteorology, which are assuming new importance. Geology, geophysics, oceanography, radio astronomy, materials research and combustion are also mentioned as needing increased support and effort.

With its limited resources, Great Britain needs to select even more carefully than the United States the objectives of her research effort; this is a task to which the Council for Scientific and Industrial Research should be giving attention before reaching its decisions about the work of its own research stations. Had there been evidence of such a wider view, particular decisions like those taken in regard to fuel research and the discontinuance of *Fuel Abstracts* might have been less open to challenge. In directing attention last year to the need for the creation of new institutions for fundamental research in particular fields or sub-fields of science, the National Science Foundation stressed the importance of obtaining ample evidence where it is thought that existing facilities are inadequate or inappropriate, and it is no less important in closing down work in a particular field to be sure that appropriate facilities exist elsewhere.

The Panel on Research Policy in this report discusses also the problem of sponsored research in non-Government institutions and recommends more consideration of programme grants as a means of reducing the potential growth of Government administration and providing greater freedom for the scientific community to direct the work. It also recognizes the importance of the independent research foundation and private industry, and the need to avoid discouraging such support of research. The climate as well as the means have to be created whereby ideas which are challenging and sound but unconventional and difficult can be hospitably considered and encouraged.

Dr. Killian refers next to the activities of a Panel on Science and Technology in Foreign Affairs which has been concerned notably with aid to under-developed countries, the re-establishment of the posts of scientific attachés, and the creation of the necessary atmosphere for effective interchange of ideas and international scientific co-operation. Again, he describes at some length the study, by the Panel on Science and Engineering Education, of the objectives and needs of that part of the educational system which is responsible for supplying adequate numbers of first-rate scientists and engineers and achieving a high degree of scientific literacy. This Panel was convinced that some of the major challenges facing the United States to-day are on the intellectual front and that, in the long run, a greater desire to learn and increased respect for intellectual excellence may be essential to national survival—a view which Dr. Warren Weaver has elaborated in an article in *The Scientific American.*

This may be equally true of Great Britain, and it is certainly true that, in considering our educational problems at any level, we, too, should be considering how such objectives can best be achieved. From this point of view alone, it is of interest to note three specific conclusions reached by this Panel. First, because in the immediate future the rising number of students will outstrip the supply of teachers, it is necessary to find new ways of increasing the effectiveness of existing teachers. Secondly, more attention should be given to the quality and content of courses and curricula in science. Thirdly, in the judgment of the Panel, in relation to national responsibilities and opportunities in science, the United States has too few first-rate institutions of higher education in science and engineering, so that there is real danger of overloading the few departments of the highest quality.

The Minister of Education, Mr. Geoffrey Lloyd, remarked in the House of Commons on March 12 that his main impression on his recent visit to the United States was that the American and British educational systems are growing closer together, and that each in its own way is seeking to combine equal educational opportunity with high academic standards, particularly for specially gifted children. The three specific conclusions of the Panel relate to American conditions but are essentially valid elsewhere, particularly if it is intended to pay greater attention to specially gifted children. Moreover, as Dr. Killian emphasizes, the quality of science and of scientific education depends on the quality of the intellectual life in the society in which they are nurtured, and his plea for adequate attention to the cultivation of talent, quality and intellectual ability is one to be heeded equally in Britain.

In reaffirming his belief in the capacity of man to improve both himself and his society, Dr. Killian rejected the note of pessimism to be found in Britain as well as in the United States. He insisted that science does not contribute simply to the comfort and convenience of life: it contributes also to its quality, to the individuality from which creative work arises, to its dignity as well as to its productivity. Science, he claimed, is one of the great disciplines vital to society and worthy of first-class minds, and the growing linkage of science and technology with government demands of science a new order of poise and statesmanship, and of the scientists who serve as advisers a deep understanding of the role and limitation of the adviser. It is only when this conception of science as one of man's most powerful means for searching out truth and augmenting his dignity is fully and widely recognized that science can prosper in any country and attract its proper complement of creative and gifted minds.

It would be foolish to suggest that the new structure for bringing science and technology to play their fitting part in public policy in the United States should be slavishly imitated in Britain. The importance to Britain of Dr. Killian's review and of the report on strengthening science in the United States lies rather in indicating factors which should receive closer attention, in suggesting points of view from which our own organization may well need re-appraisal, dangers to be avoided and problems on which new and creative thinking is required. The emphasis on education is to be noted above all, for on that finally depends both the effectiveness with which science and technical advice is presented and the understanding with which it is received. Whatever criticisms may well be made as to the shortcomings of the British organization for bringing science to bear on public policy, the address which the Prime Minister gave to the Parliamentary and Scientific Committee at its annual luncheon on February 18 shows how largely this is already recognized.

Mr. Macmillan referred to the opportunities he had of listening to scientific advice, particularly in view of his departmental responsibility for the Atomic Energy Authority, and to the Government's duty to increase the scientific potential, including the provision of sufficient trained man-power through the educational system and the development of scientific and technological teaching in the schools, technical colleges and universities, as well as the provision of adequate and varied facilities for research. With his reference to the importance of international co-operation in this field, including the decision at Montreal to establish an Overseas Research Council, Mr. Macmillan's address showed that attention is already being given to the several aspects of Government support for science and technology discussed by Dr. Killian, and if the scale of that support can sometimes be challenged, the Government is at any rate aware of a responsibility. Mr. Macmillan pointed out that a Minister has, in fact, much in common with the scientist: like him, he must always be ready to study and use all known facts bearing on a problem; to search dispassionately for truth and right answers; and to be ready to recognize them when the facts force them on our understanding, whatever the cost to our previous beliefs or prejudices. No scientist could ask or expect more than that a Minister should show the courage and vision to act on such principles, or that a Government should be, as Mr. Macmillan affirmed, alert to such scientific advice, not only about what it is doing now, but also about what it might be doing five, ten or twenty years hence. Mr. Macmillan's address to the Parliamentary and Scientific Committee should encourage the scientist and technologist to examine and explore the possibilities of improving our research organization, our advisory services and our educational system; Dr. Killian's review of the work of the Science Advisory Committee may suggest with greater confidence that the task will be well worth while.

GREAT THINKING

The Physicist's Conception of Nature

By Prof. Werner Heisenberg. Pp. 192. (London: Hutchinson and Co. (Publishers), Ltd., 1958.) 16*s*. net.

Atomic Physics and Human Knowledge

By Dr. Niels Bohr. Pp. viii+101. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 32*s*. net.

Science Theory and Man

By Erwin Schroedinger. Formerly published under the title "Science and the Human Temperament". Pp. 223. (London: George Allen and Unwin, Ltd., 1957.) 18*s*. net.

Mind and Matter

By Prof. Erwin Schrödinger. (The Tarner Lectures delivered at Trinity College, Cambridge, in October 1956.) Pp. vii+104. (Cambridge: At the University Press, 1958.) 13*s*. 6*d*. net.

A LARGE part of Prof. Heisenberg's book is entitled "Historical Sources", and consists of long quotations of great writers on physical science from Kepler to Louis de Broglie. These are selected to show the "changes in the attitude of science" that have occurred during the development of 'modern' science. Needless to say, a selection from such great thinkers made by another great thinker is in itself of profound interest. But it immediately occurs to one that we have before us some of the writings of three of the greatest contributors to the latest phase of the development; one wonders how another Heisenberg of, say, 300 years hence might quote from them in making a corresponding selection for his own time and how true an impression of this phase would be given thereby. This in turn makes one wonder what is the real significance of a selection such as Heisenberg himself has made.

The first point that seems relevant to these considerations is somewhat prosaic. Some of the contents of these books are invited addresses for various public occasions. The very care that the authors have taken to suit their particular audiences hinders them from being wholly 'professional' accounts of their subjects. Far more, one questions whether, for example, Heisenberg's first quotation from the dedication of the "Mysterium Cosmographicum" to "their Illustrious, High-born, Noble and Righteous Lords . . ." should be treated critically as the record of Kepler's scientific attitude. Again, the most fascinating parts of Prof. Schrödinger's books are his personal reflexions upon the perennial problems of the place of science in human thought; they largely transcend the particular phase of physical science to which he has contributed. Similarly, one asks if, for example, Heisenberg's quotations from W. Ostwald, who was a less inspired thinker and writer than Schrödinger, are more than his personal reflexions and if they serve to give a just indication of the contemporary trend of physical thought.

Of the dozen writers quoted by Heisenberg, probably only Galileo, Newton and de Broglie have themselves made advances in the most fundamental development of physics more important than, or as important as, those made by the three authors of the present books. Moreover, it happens that these authors have written here and elsewhere with very deep penetration about the significance of the developments to which they have contributed so much.

In passing, we may learn something from the fact that Heisenberg quotes nothing from Hamilton, Faraday, Maxwell or Rutherford, whose work contributed vastly more to the development of physics than that of the majority of writers on his list. It is that physics itself is just what it is gradually discovered to be, and physicists who are prepared to take it, literally, as they find it are able to make great progress. If it be contrary to their cast of mind to trouble much about questions of significance, that probably makes no difference to their strictly scientific work. This is almost inevitably the case, since advances come by not over-rating the significance of previous work and they have to come before their own significance can be discussed. The attitude of such physicists towards their work is akin to that of a pure mathematician in his field.

Nevertheless, for most of us it is a truism that the interest of scientific advances is in what we call their significance; and what Bohr, Heisenberg and Schrödinger are doing is to stand back from their own work in order to survey its setting in wider fields of thought and its possible influence upon such thought. Bohr's book is a collection of essays and addresses prepared over the years 1932–57, and they have all had extreme care bestowed upon them. The author says himself, "The theme . . . is the epistemological lesson which the modern development of atomic physics has given us and its relevance for analysis and synthesis in many fields of human knowledge". Heisenberg's book consists, in the first part, of a sketch of the attitude to Nature in modern physics, together with general considerations regarding intellectual problems confronting man in the situation produced by the development of his own science and technology. The second part consists of the "sources" already mentioned, which are claimed to show that modern science started with an awareness of the limitations of its scope, passed through a phase in which it forgot its own limitations, and is now appreciating these limitations with new insight. The first of Schrödinger's books is a re-issue, with one addition, of the essays previously published in "Science and the Human Temperament" (1935). His second book consists of the Tarner Lectures for 1956. It is the most far-ranging of all these books and, in one way or another, bears upon the whole range of human thought. To the reviewer it breathes a freer air than do the others. This is perhaps because Schrödinger seems less prone to regard recent developments as supremely decisive in the long roll of man's thinking and so it comes more naturally to him to look beyond them. Whereas Heisenberg says, "When we speak of the picture of nature in the exact science of our age, we do not mean a picture of nature so much as a *picture of our relationships with nature*", Schrödinger says, "The world is given to me only once, not one existing and one perceived. Subject and object are only one. The barrier between them cannot be said to have broken down as a result of recent experience in the physical sciences, for this barrier does not exist".

However, when these distinguished authors stand back to survey the whole realm of thought, it cannot be expected of the writer of a short review to stand even farther back to survey the survey. All he can do is to urge others to enjoy the extraordinary richness of thought contained in each of these brief volumes.

W. H. McCrea

ADVANCES IN MICROBIOLOGY

Annual Review of Microbiology

Vol. 12. Edited by Charles E. Clifton in association with Sidney Raffel and Mortimer P. Starr. Pp. viii + 579. (Palo Alto, Calif.: Annual Reviews, Inc., 1958.) 7 dollars.

In these days when the expanding volume of literature is the despair of every scientist who hopes to keep abreast of advance in anything more than a narrow field, the annual review volumes have become indispensable. They serve two purposes: to provide a rapid guide to recent literature and, more rarely, to present an appreciation and synthesis of recently acquired knowledge. The latter type of review article is only possible when knowledge in a particular branch has reached a degree of attainment and significance that enables something more than appraisal of detail to be attempted. Three of the major articles in the present "Annual Review of Microbiology" are in this latter class and each makes a valuable contribution in its own right: "Metabolism of Carbohydrates and Related Compounds" by S. R. Elsden and J. L. Peel is an outstanding contribution, particularly in its consideration of the energetics of anaerobic metabolism, discussing the breakdown of substrates from the point of view of the yield of adenosine triphosphate. The article also covers cellulose synthesis and breakdown, the breakdown of aromatic compounds, and tricarboxylic acid cycles. "Bacterial Genetics" by A. W. Ravin reviews advances on the mutation, replication, transfer and function of genetic material, and the contribution by A. Nason and H. Takahashi places recent studies on denitrification, nitrate utilization, nitrification and nitrogen fixation into perspective in the field of "Inorganic Nitrogen Metabolism".

"Bacterial Protoplasts" and "Bacterial Viruses" are dealt with by C. Weibull and W. Weidel, respectively, while L. Provasoli presents a thoughtful study of the relation between laboratory and field investigations in the "Nutrition and Ecology of Protozoa and Algae". The parasitic and pathogenicity aspects of microbiology are well catered for in this volume, which contains reviews on staphylococci, respiratory tract viruses, virus infection in plants, parasitic diseases in man, and the use of bacteria grown *in vivo* for studies on the basis of their pathogenicity. The control of infection is discussed in articles on antibiotics in plant disease, chemical disinfectants, and radiation preservation of food. P. Grabar provides a further summary, with 200 references, of recent Russian literature.

It can be seen that the present volume, containing nineteen articles and a grand total of 3,211 references, will find a place on the shelves of microbiologists, medical men and biochemists, all of whom will acknowledge their indebtedness to the editors and contributors for maintaining the high standard that we have come to expect of these "Annual Reviews".

TOPICS IN CARBOHYDRATE CHEMISTRY

Polysaccharides in Biology

Transactions of the Second Conference, April 25, 26 and 27, 1956, Princeton, N.J. Edited by Dr. George F. Springer. Pp. 245. (New York: Josiah Macy, Jr. Foundation, 1957.) 5 dollars.

This book gives a verbatim account of the transactions of a second conference, sponsored by the Josiah Macy, Jr. Foundation. It brought together a group of experts who discussed three topics in carbohydrate chemistry, namely: "Sialic Acid and Related Compounds"; "Interaction of Polysaccharides and Viruses"; and "Pyrogens". These topics are of the utmost importance in certain aspects of medicine at the present time, and the twenty-six experts were undoubtedly among the best that could be got together for the particular subjects. The method of reporting the conference, however, must be sharply criticized, because it can only be of value to the expert: even to the expert it is very irritating, but to the non-specialist it would be almost impossible to get anything of real significance out of the book. The whole thing is reported in a completely uncritical manner, and many comments of the experts, some of them mere interjections, are of no value. Perhaps the scientific editors will in future take a leaf out of the books of the Ciba Foundation and provide a substantial piece of well-thought-out writing on which to base the main conclusions of a topic: then comments by participants in the succeeding discussion will have more weight and will be more tangible.

The discussion on sialic acid and related compounds was led by Dr. F. Zilliken, and generally all that is known about this interesting group of substances up to 1956 was brought out either by direct communication or by discussion. The growing importance of this nonosaminic acid was well illustrated by the experiences of the participants in a number of fields.

The discussion of polysaccharides and viruses was led by Frank L. Horsfall, who was allowed to make at least a page and a half of contribution before he was interrupted by his fellows. It did emerge that the twenty or more viruses react in one way or another with erythrocytes. Many of them can cause hæmagglutination, a phenomenon which can be inhibited specifically by complex polysaccharides of the muco-protein class. Powerful inhibitors of viral hæmagglutination may be found in urine, egg-white, serum, and so on. The animal viruses may be divided into three groups: those which contain particles which react with the red cells, are absorbed, and then emerge again; others which contain components which react and are absorbed by the red cell but cannot be released; and the third group which does not attach itself to a red cell but produces a soluble substance that does attack the cell.

The discussions on the implications of these new interactions of polysaccharides and viruses components are intensely interesting. The discussion on pyrogens was led by Dr. O. Westphal, of the Wander Research Institute, Freiburg, Germany. Pyrogens are substances which, after injection in higher animals, promote a rise in body temperature. Among these are many polysaccharides, particularly those which are elaborated by bacteria. The problem of pyrogen production is, of course, of the greatest importance in medical treatment. Those discussed were of the lipo–polysaccharide–protein complex type. In this discussion masses of observations by the different participants were described and in one way or another almost all the constituents of Gram-negative bacteria have been brought in. The nature of the properdin system and its reaction with polysaccharides were well discussed and comparisons were made between properdin and antibody. In some cases these are well described in tables and diagrams, but they are very difficult to sort out in regard to their relative importance.

Excellent references are given, and to the expert, the whole of this discussion will be of the greatest value and interest. However, to make the book of wider appeal and the discussions of greater value in the future, it is to be hoped that the editor will make a critical assessment of those positive results which have emerged from discussion.

M. Stacey

POPULATION ECOLOGY

Animal Ecology To-Day

By Prof. F. S. Bodenheimer. (Monographiae Biologicae, Vol. 6.) Pp. 276. (Den Haag: Uitgeverij Dr. W. Junk, 1958.) n.p.

Cold Spring Harbor Symposia on Quantitative Biology

Vol. XXII: Population Studies—Animal Ecology and Demography. Pp. xiv+437. (Cold Spring Harbor, L.I.: Long Island Biological Association, 1957.) 8 dollars.

Bodenheimer's "Problems of Animal Ecology" (1938) has for some time been out of print. Although broader in scope, "Animal Ecology To-Day" is essentially a revision of the earlier book in the light of twenty years added experience. The central theme remains that "the principal aim of ecological research is to explore the fluctuation of populations and their (homologous) causes". From this point of view Bodenheimer discusses longevity (Chapter 1), life-history (2), population dynamics (3 and 4), the community (5), environment and heredity (6) in animals, and ends with a brief dissertation on human ecology (7). Many of the illustrations are from works unfamiliar to Western readers. As might be expected in a widely ranging treatise, a few subsections are not quite up to date.

"Animal Ecology To-Day" is truly, as the author says, "not written against anyone or against any theory" quoted or discussed. Nevertheless, it is still to a considerable extent a fairly strong testament of Bodenheimer's personal views. Naturally, he has changed some of the latter since 1938; for example, on the question of weather in population dynamics. At the same time, he is sometimes penetratingly critical of opposing views, as when he points out that parasites can be wrongly credited with controlling increase of their hosts (Fig. 17). This is not a book for beginners. It should be regarded as a thought-provoking supplement to text-books such as those of Allee *et al.* and Andrewartha and Birch. The mature ecologist will find much with which to agree and much with which to disagree. Where acceptable it is sometimes illuminating, and where unacceptable it is occasionally stimulating. Theorists, and those who do not readily distinguish between theory and fact, should profit by reading pp. 190–201.

For up-to-date comprehensive surveys, biologists the world over owe much to the organizers of the carefully edited and beautifully produced "Cold Spring Harbor Symposia". Vol. 22, on population studies, puts them still further in debt. No serious worker on population problems can afford to be without access to it. Containing thirty-six papers (with useful discussions of twenty-four), it is devoted about equally to human and animal populations. Many of the authors are well-known authorities in their subjects and about one-third are from outside the North American continent. Representation is well balanced with respect to controversial matters; for example, the question of natural control of animal populations. Beginning with a very capable introductory survey (containing, as seems to be inevitable, its author's own views at some length), the volume effectively covers most of the important aspects of population study—historical, theoretical, laboratory and field. One is still waiting, however, for geneticists to direct their attention from evolution to regulation of populations. Like all symposia (cp. "The Numbers of Man and Animals"), this volume has disjointed and ill-assorted features. One therefore admires the realism of the author of the "Conclusion", who soon abandons all pretence of summing up the proceedings and devotes most of his paper to expounding a particular view of his own. After all, no one could be expected to sum up proceedings on two subjects so different (despite some basic similarities) as human and animal populations, and including papers on aspects as diverse as "Farris' Formula for predicting Fertile Days" in women and "Roosting Habits, Sexual Dominance and Survival in the Great Tit". Future symposia should be on either human or animal populations, but not on both.

In animal ecology to-day there is less need for new books than for an international committee to define and standardize terms and concepts. Perusal of these two volumes makes this abundantly clear.

A. Milne

Hemophilia and Hemophilioid Diseases

International Symposium. Edited by Prof. Kenneth M. Brinkhous. Pp. xxii+265. (Chapel Hill, N.C.: University of North Carolina Press; London: Oxford University Press, 1957.) 60*s*. net.

In August 1956 a symposium, sponsored by the National Hemophilia Foundation of the United States, was held in New York. About 125 persons attended, and among the 62 who read papers or contributed to the discussion were included a high proportion of the scientists and clinicians of the present day who have contributed most to the study of hæmophilia and allied disorders. The present book is a record of this meeting, consisting of 29 papers divided into seven main sections and verbatim reports on subsequent discussions. Most of the papers are illustrated by figures and most of them include adequate lists of references.

The papers are inevitably of uneven quality; some are short general summaries, others describe experiments in detail. One of the most interesting and controversial subjects discussed inconclusively at the symposium was the frequency with which anticoagulants or inhibitors are found in the plasma of hæmophiliacs and their importance in the pathogenesis of bleeding. The discussion at the end of each group of papers makes interesting reading, even if the questions asked and statements made often pose more questions than they answer.

A good example of a tantalizing statement is to be found at the foot of p. 62. In it R. J. Carroll states that hæmophiliacs are graded 1, 2, 3 and 4 on the basis of the anticoagulant content of their plasma and that the grade is constant for a particular patient. It need perhaps scarcely be added that there is still no uniformity of opinion as to whether anticoagulants really exist in hæmophilic plasma except on rare occasions.

This is a book for those who have a special interest in the hæmorrhagic disorders, whether they be physicians, clinical pathologists or medical scientists. It does not seem likely to have much appeal to workers outside this field.

J. V. Dacie

Biological Aspects of the Transmission of Disease

Edited by C. Horton-Smith. (Reports of Symposia of the Institute of Biology.) Pp. ix+184. (Edinburgh and London: Oliver and Boyd, Ltd., 1957. Published for the Institute of Biology.) 21*s*. net.

"Biological Aspects of the Transmission of Disease" is the title of the proceedings of symposia organized by the Institute of Biology. It covers such a wide range of subjects that few reviewers would feel competent to do it justice. With the increasing specialization in all aspects of biology, it is very refreshing and most instructive to read accounts of problems of transmission of disease in fields or media totally different from those known to the reader.

As is inevitable in asking experts to write briefly on very complex subjects, one can find minor errors and ambiguity in places, but this does not really detract from the value of this kind of book in widening the field of interest and, one hopes, whetting the appetite of the reader to pursue further many original papers by the eminent contributors.

Unfortunately, it is a small book for a guinea.

C. W. Dixon

The Astronomer's Universe

By Prof. Bart J. Bok. Pp. xi+107+16 plates. (Melbourne: University of Melbourne Press; London: Cambridge University Press, 1958.) 21*s*. net.

The author of this book, who was formerly on the staff of the Harvard Observatory, is now director of the Commonwealth Observatory and professor of astronomy in the Australian National Observatory. The book is based on four lectures delivered in Canberra, in which some account was given of the more important developments that have been made in recent years in our knowledge of the universe. The first of these lectures deals with some problems of the solar system, including the atmospheres of the planets, the origin of the system, and the Sun's corona. The second is concerned with some of the properties of stars as individuals and describes the two types of stellar populations found, respectively, in the spiral arms of galaxies, and in stellar clusters and galactic nuclei. The third lecture is concerned with the Milky Way system and summarizes the evidence for the existence of spiral arms from optical and radio observations. The final lecture is somewhat more speculative in character, discussing matters, such as the cosmic time-scale, stellar evolution, and the birth of stars, on which much evidence has been obtained in the past decade.

The book avoids technicalities and is well written. It will interest all who wish to know how astronomical ideas are tending in many important problems which still await definite solutions. The book, which was printed in Melbourne, is well produced and has reproductions of a number of stellar photographs, several of which were obtained at the Commonwealth Observatory.

H. Spencer Jones

Physical Acoustics and the Properties of Solids

By Dr. Warren P. Mason. (The Bell Telephone Laboratories Series.) Pp. xii+402. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1958.) 67*s*. 6*d*.

Workers in acoustics look forward eagerly to a new book from the pen of Dr. W. P. Mason, who brings to his writings the authority and experience of many years on the research staff of the Bell Telephone Laboratories. As head of mechanics research he is writing of his own work and that of his associates in the main, though with frequent comparison of the Bell methods with those of other laboratories. The title of the book is possibly a little misleading since the words "physical acoustics" are evidently to be taken in conjunction with the words that follow—the introduction gives, in fact, the basic theory only in reference to the propagation of sound waves in solids.

The experimental portion covers in four chapters the sources (mostly ultrasonic) which can be used for transmitting longitudinal or shear waves in bars, the method of determining the velocity and attenuation of the signals launched into them, together with industrial applications of these experiments, like the ultrasonic flaw detector and the soldering iron, for which British firms have gained credit.

Part 2 of the book will have most appeal to physicists, since it discusses the theory of transmission of these waves in terms of dislocations, grain boundary losses, and lattice vibrations with their relaxations. The general reader can, in fact, appreciate from this authoritative account the important part which acoustics is playing to-day in solid state physics.

E. G. Richardson

SOCIAL IMPLICATIONS OF MENDELISM VERSUS MICHURINISM

By A. QUINTANILHA

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THE rediscovery of Mendel's Laws in 1900 raised the greatest interest in the world of science. Such a great amount of knowledge on the behaviour of the chromosomes, in the somatic life as well as in the sexual reproduction of plants and animals, accumulated during the last twenty years of the nineteenth century that it was not difficult to find a perfect parallel between this behaviour, on one hand, and the transmission of hereditary units, on the other. Thus was born the chromosome theory of heredity, an eminently materialistic theory which tried to localize in material particles, along the chromosomes, the factors responsible for the transmission of those hereditary characters which follow Mendel's Laws.

However, the fact that the first Mendelian geneticists were essentially interested in the problem of transmission of hereditary characters, that is, in the phenomenon of permanence, throughout the generations, of characters already existent in the ancestors, caused a great number of biologists and a considerable part of public opinion to suspect that the geneticists of the then new school were anti-evolutionists and reactionaries. This suspicion was reinforced by the fact that Mendel was a Catholic priest; and, on the other hand, by the circumstance that the Mendelian geneticists did not accept the Lamarckian theory of the heredity of acquired characters.

But after the first years of confusion the situation became clearer. The new school of Mendelian genetics accepted, as a demonstrated fact, the doctrine of evolution; and, as all the experiments trying to demonstrate the heredity of acquired characters led to negative results, they looked for the explanation of evolution in spontaneous mutability and natural selection.

In 1935, Lysenko started a campaign, partly scientific and partly political, against Mendelian genetics. Using, and, in my view, abusing, the name of Michurin, who enjoyed great popular prestige in the U.S.S.R., Lysenko tried to create a new school of Soviet biology of a strong nationalistic and anti-Mendelian tendency.

Mendel's fundamental and most original idea is that there are independent units of heredity responsible for the transmission of those characters which follow mathematical laws. The followers of Mendel succeeded in demonstrating that such units really exist, and are material particles localized in the chromosomes.

The Michurinists, on the contrary, deny the existence of cellular organs responsible for the transmission of hereditary characters. Heredity, they say, is a function of the organism as a whole, and not of any one specific organ. In grafting, for example, the scion as well as the stock can transmit to one another hereditary characters by means of plastic substances. "The plastic substances", wrote Lysenko, "produced by the scion and the stock, possess the characters of the breed, are endowed with definite heredity just as the chromosomes, and just as any particle of the living body"[1].

The Michurinist theory seems to me, on this point, in complete disagreement with the coherent results of half a century of cytogenetic research. To deny the specific role of the chromosomes in transmission of those hereditary characters which obey Mendel's Laws would be as absurd as to deny the specific role of the chloroplasts in carbon assimilation in green plants.

But the most interesting aspect of the question is that Michurin himself was not a Michurinist in the same sense as Lysenko. He himself confesses: "Unfortunately, I at first was enthusiastic about Grell's ideas of those days concerning the acclimatization of the best foreign varieties by grafting them on to hardy wild plants. Much labour and time were lost on these erroneous experiments before I finally became convinced that the method was useless. Then, following the advice of Dr. Betling, I began to breed my own new local varieties of fruit-bearing plants from the seeds of superior quality fruits. But it soon became clear to me that I could not expect to accomplish much without artificially crossing local varieties of plants with the best foreign varieties, because it is difficult to obtain higher qualities from mediocre varieties. To achieve this, the fruit of one of the parent plants must possess better, outstanding qualities. Consequently, it was necessary to resort to hybridization"[2].

That is, while Michurin used the Lamarckian methods of progressive acclimatization of varieties from temperate climates to the hard conditions of central Russia, he had only failures. Then he started working as any plant breeder of the Mendelian school would, that is, crossing varieties highly resistant to cold with others from temperate climates, not resistant but producing fruits of outstanding quality, and selecting among the descendants those plants bearing a new and desirable association of characters. Michurin was then acting as if he accepted the Mendelian principle of the existence of independent hereditary units susceptible of being associated in new combinations. He was carrying out Mendelian plant breeding.

Moreover, the impression which one gets from reading Michurin's "Selected Works" and from his biography is that he was a modest man without any kind of pretension to create a new biological doctrine and without the aggressiveness characteristic of the writings of his disciple and admirer, Lysenko. His criticism of the Mendelian theories is, above all, the consequence of a deficient scientific education. As a self-taught man, Michurin must have met with enormous difficulties in access to works of reference, and it is highly probable that he never read Mendel's original work.

In an article published in 1925, in which he gives a summary of the results of half a century's work, he says: "In conclusion, I should like to note that in general, and in the brief résumé of my work in particular, I make no pretensions of having demonstrated new discoveries or having refuted any laws established by authorities in science.

"It is very probable that in some cases I may be wrong due to having erroneously interpreted various phenomena in the life of plants and the application of, let us say, the laws of Mendel or other modern teachings to them; but such mistakes are inevitable in every work and they cannot be of much significance since they will in all probability be rectified by other investigators in the future"[3].

It is strange to notice that the Michurinists accept enthusiastically and with great praise Darwin's materialistic theory of evolution with the exception of its most original part, the principle of natural selection, as a consequence of the struggle for life, and the survival of the best adapted. Yet, strange though this may seem, it can be explained. Darwin himself confesses: "In October 1838, that is fifteen months after I had begun my systematic inquiry, I happened to read for amusement *Malthus on Population*, and, being well prepared to appreciate the struggle for existence which everywhere goes on from long continued observation of the habits of animals and plants, it at once struck me that under these circumstances favourable variations would tend to be preserved, and unfavourable ones to be destroyed . . . Here then I had at last got a theory by which to work"[4].

Now the work of Malthus was published for the first time in 1798 in an atmosphere of controversy. Against the socialist doctrine that misery is a consequence of a faulty social organization, Malthus tried to prove that, on the contrary, misery was the necessary consequence of a natural law, the law which rules the growth of population. When there are no obstacles, the human population, like those of other animals, tends to grow in geometric progression, while the means of subsistence grow in arithmetic progression.

Misery in the last analysis is the unavoidable consequence of this disproportion, of this 'natural law'. Great famines, wars, epidemics, social or natural cataclysms are so many other means which re-establish automatically a certain equilibrium between the number of mouths and the possibility of feeding them.

Social reforms, raising the standard of living of the poorer classes, far from solving the fundamental problem, may even help to aggravate the situation; as a matter of fact, stimulating the birth-rate of the working classes by a temporary increase in their well-being may create in this way a greater future discrepancy between the population and the means of subsistence.

For Malthus the problem is not a social one, and it is not possible to solve it by re-organizing human society on different bases. The only solution would be the exercise of 'moral restraint'—abstention from marriage for poor people who could not feed and educate their families, and the practice of conjugal continence for married people in similar conditions.

The application of Malthusian principles to animals and plants allowed Darwin to find an explanation of evolution, that is, the appearance of new species derived from pre-existent ones. An unavoidable consequence of the population law is the struggle for life, for breathing space and means of subsistence between individuals of the same species. As soon as the species covers a sufficiently large area, in each place there will be greater probability of survival for individuals bearing variations which make them better adapted to the local conditions. From this arises the tendency for the formation, inside the species and in different ecological areas, of nuclei of populations with different hereditary characters, each of which is the possible starting point for the formation of a new species.

During the nineteenth century, economists and sociologists tried to use Malthus's doctrine against socialist propaganda. In the same way Darwin's theory of the struggle for life and the survival of the fittest was used to justify the existence of human societies divided into classes with different functions and different rights.

Competition, the struggle for life among individuals of the same species, would be in this way a natural law from which human society could not escape. Just as in other animal societies, the struggle for life among human beings would lead to the success of the fittest. It would then be quite in order to give the upper classes functions of direction. Misery, hunger, unemployment are not only unavoidable consequences of biological laws; but in their way they contribute to the slowing-down of procreation in the worst-adapted classes of society.

It is not difficult to understand the violence of the reaction in socialist circles, not only against Malthus's doctrine on population, but also against the political-social consequences which sociologists pretended to deduce from Malthus's and Darwin's doctrines.

Karl Marx, in his famous book "Das Kapital", attacked Malthus sharply and asserted that an abstract law of population can only exist for plants and animals. In human societies a particular law of population corresponds to each type of social organization of production. In the capitalist society of the nineteenth century, the limiting factor in population increase was the possibility of obtaining work. The working classes were permanently under the menace of unemployment crises, an unavoidable consequence of a social organization which produced not for consumption but for sale.

Engels's reaction was not less violent, and extended to the consequences which, in reactionary circles, they pretended to deduce from Darwin's doctrines. In a letter published in 1875 he wrote: "The entire Darwinian teaching on the struggle for existence merely transfers from society to the realm of living nature Hobbes' teaching on *bellum omnium contra omnes* and the bourgeois economic teaching on competition, along with Malthus' population theory. After this trick (the absolute justification for which, as indicated in point 1, I deny, particularly in regard to Malthus' theory) has been performed, the same theories are transferred back from organic nature to history and the claim is then made that it has been proved that they have the force of eternal laws of human society. The childishness of this procedure is obvious, and it is not worth while wasting words on it. But if I were to dwell on this at greater length, I should have started out by showing that they are poor economists first, and only then that they are poor naturalists and philosophers"[5].

Kautsky accepted the Malthusian principle that human populations, like animal ones, *tend* to grow quicker than the amount of available food. But, like Marx, he directed attention to the circumstances that, in capitalist societies, what limits the production is the antagonism of interests between the proprietors and the workers. Once this antagonism disappears through the advent of socialism, the production of means of subsistence will be able to increase in unprecedented proportions. But, according to Kautsky, this will not yet solve the problem, because the tendency of a more rapid increase in population than in the means of subsistence will remain. The solution, however, is not in the abstention from marriage nor in the practice of continence, as Malthus preached, but in a future birth-control. Already in 1880 Kautsky foresaw that birth-control would be more and more used as the cultural level of human society rose.

The solution of the tragic problem posed by Malthus at the end of the eighteenth century is then, for Kautsky, in the advent of socialism and in the practice of birth-control.

Another great socialist who wrote widely about the problem was Kropotkin. In his book "Mutual Aid as a Factor of Evolution", Kropotkin tried to demonstrate that, besides the struggle for life among individuals of the same species, another factor of evolution exists, namely, mutual aid. In animal populations, as soon as social life becomes intensified, there develops a spirit of co-operation and solidarity. The struggle of one against all for the means of subsistence tends to be little by little replaced by the struggle of all the individuals of the same society against their common enemies and against adverse natural conditions.

As soon as animals start to live in societies a new factor intervenes in natural selection, namely, the instinct of sociability (gregariousness). Within each species Nature will select those individuals in which this instinct is most highly developed. In inter-specific competition, those species in which social life is best organized will have greater chances of success.

Many other socialist leaders took an active part in the controversy which arose around the thesis put forward by Malthus and the social consequences which many sociologists pretended to take from his doctrines and from that part of Darwin's theory of Malthusian origin.

Now we can understand better the attitude of the Michurinists who, imbued with an out-of-date Marxism, were never able to understand that the admission of the existence of a struggle for life between individuals of the same species, in the plant and animal kingdoms, does not in any way justify the social consequences which the opponents of socialism pretend to deduce against the socialist doctrine.

In the plant kingdom and in a great number of animal species the struggle for life, even among individuals of the same species, is a biological fact so evident that it seems to me difficult to deny it. But already in many animal species, as soon as a social life starts, this struggle begins to be gradually replaced by co-operation between the members of the same community against their external enemies and the adverse conditions of Nature: and who would be better placed than the Russian biologists to assert that, in human societies, it is possible and advantageous to replace the principle of competition between individuals of the same community by the principles of co-operation and mutual aid?

Modern history proved the correctness of the socialist leaders' predictions in the Malthusian controversy. In modern human societies the reproduction-rate decreases, in spite of the spectacular decrease in mortality, with the increase in their cultural level. Deliberate birth-control tends, therefore, to establish an automatic balance between the number of mouths to be fed and the possibility of feeding them. On the other hand, the advent of socialism and consequent disappearance of antagonistic class interests has shown the possibility of developing agricultural and industrial production, even in backward countries, in a way without precedent in human history.

The rejection by the Michurinists of the Darwinian doctrine of the struggle for life as a factor of evolution is, in my opinion, the consequence of a social–political prejudice, the erroneous conviction of the incompatibility between that doctrine and the socialist ideal of a classless society based on the principle of co-operation.

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DENSITY OF THE ATMOSPHERE AT HEIGHTS BETWEEN 200 KM. AND 400 KM., FROM ANALYSIS OF ARTIFICIAL SATELLITE ORBITS

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THE action of atmospheric drag makes the orbit of an Earth satellite slowly contract, and its period of revolution T decrease. When the eccentricity of the orbit exceeds about 0·02, the drag at perigee is much greater than at apogee, and the rate of decrease of T is determined by the total loss in velocity due to the integrated effect of drag in the region near perigee. If the mass and dimensions of the satellite are known, and estimates are made of its aerodynamic drag, values of air density at heights near perigee can be obtained.

Such estimates of air density have been made in a number of previous papers[1–11]. Since the effective cross-sectional areas and drag coefficients of the satellites are difficult to determine exactly, the various authors have inevitably made different estimates of these quantities. Also most of the previous papers refer to only one or two satellites. In the present article, values of density are derived from all the ten satellites launched up to the end of 1958 whose orbits are known, the satellites are treated consistently, and a more accurate method of determining density is used.

Previous Estimates

The results from the previous papers[1–11], and values[12] obtained from instruments aboard *Sputnik* 3 (1958 δ 2), are collected in Fig. 1, together with two proposed interim model atmospheres[3,13] and the A.R.D.C. model atmosphere[14], which was probably the most widely used standard atmosphere in the year prior to satellite launchings. As is well known, the results from satellites show the density in the

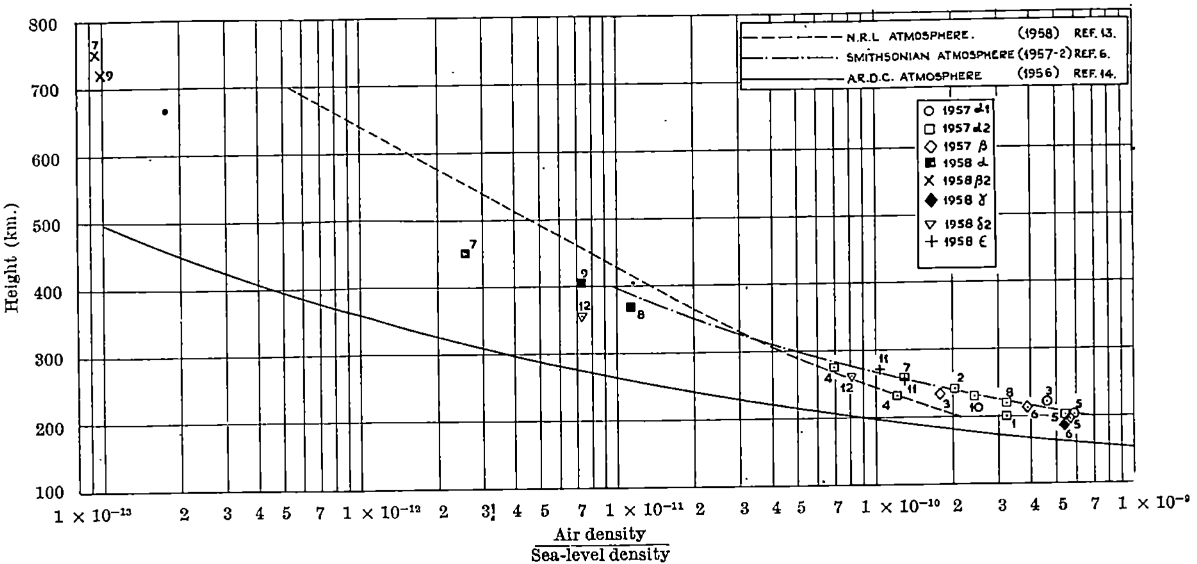

Fig. 1. Values of air density obtained by means of satellites (refs. 1–12), with proposed 'standard atmospheres' (refs. 6, 13, 14). Reference numbers are shown beside the plotted points

200–400 km. height range to be 5–15 times greater than indicated by the A.R.D.C. model. In Fig. 1, the abscissa is the density relative to sea level, the sea-level density being taken as 1·23 kgm./m.^{3} or 0·0765 lb./cu. ft. The scatter of the points in Fig. 1 is not significant, since it could be due to the different methods and assumptions of the different investigators.

Present Method of Analysis

It is customary to express the air drag D encountered by a body moving with velocity v in air of density ρ in terms of a drag coefficient C_D as:

$$D = \tfrac{1}{2}\rho v^2 S C_D \qquad (1)$$

where S is a reference area, which may here be taken as the mean cross-section of the satellite perpendicular to the direction of motion. If a satellite of mass m is in an orbit with semi-major axis a and eccentricity e between 0·015 and 0·15, the air density at perigee, ρ_p, can be expressed[5,15] as:

$$\rho_p = -\frac{dT}{dt}\,\frac{m}{3\,SC_D}\sqrt{\frac{2e}{\pi a H}}\left\{1 - 2e - \frac{H}{8ae} + 0\left(e^2, \frac{H^2}{a^2e^2}\right)\right\} \qquad (2)$$

where dT/dt is the rate of change of the period of revolution T, which can be determined accurately from observation. In deriving equation 2, it is assumed that, above perigee height y_p, the density of the air varies exponentially with height, the density ρ at height y ($> y_p$) being given by:

$$\rho = \rho_p \exp\left\{-\frac{y - y_p}{H}\right\} \qquad (3)$$

where H is constant. Since the value of H is not accurately known at heights of 200–400 km., equation 2, though it determines $\rho_p\sqrt{H}$ with little error, does not yield an accurate value of ρ_p.

This limitation can, however, be avoided. Let H^* be the best estimate of H. Then the density at height $y_p + 0{\cdot}5H^*$ may, by means of equations 3 and 2, be expressed as:

$$\rho_{p+0\cdot5H^*} = \rho_p \exp\left(-\frac{H^*}{2H}\right)$$
$$= -\frac{dT}{dt}\,\frac{m}{3\,SC_D}\sqrt{\frac{2e}{\pi a H^*}}\left[\sqrt{\frac{H^*}{H}}\exp\left(-\frac{H^*}{2H}\right)\right]\left\{1 - 2e - \frac{H^*}{8ae} + 0\left(e^2, \frac{H^2}{a^2e^2}\right)\right\} \qquad (4)$$

The function in square brackets is insensitive to the value of H^*/H, and may be taken as 0·593, with error less than 2·5 per cent, if the estimated value H^* does not differ from the true value H by a factor of more than 1·5. Since H is usually known to within a factor of 1·5, and since the likely error in m/SC_D is as a rule appreciably greater than 2·5 per cent, it is legitimate to replace the term in square brackets in equation 4 by this constant, so that (4) becomes:

$$\rho_{p+0\cdot5H^*} = -\frac{0{\cdot}158\,m}{SC_D}\,\frac{dT}{dt}\sqrt{\frac{e}{aH^*}}\left\{1 - 2e - \frac{H^*}{8ae} + 0\left(e^2, \frac{H^2}{a^2e^2}\right)\right\} \qquad (5)$$

The error arising from neglect of terms in e^2 and H^2/a^2e^2 is less than 3·5 per cent if $0{\cdot}015 < e < 0{\cdot}15$. The use of equation 5 to obtain the density at height $0{\cdot}5H^*$ above perigee should not lead to errors of more than 4·5 per cent if H^* is not in error by a factor of more than 1·5. If H^* is in error by a factor of 2, the error in equation 5 rises to 12 per cent.

Evaluation of m/SC_D

In applying equation 5 to actual satellites, the chief difficulty is the evaluation of SC_D. Its value depends on the shape of the satellite, the manner in which it is rotating, and the mechanism of reflexion of the air molecules. Diffuse reflexion, in which the air molecules are re-emitted in a random manner after striking the surface, has been chosen as the most likely mechanism, in preference to specular reflexion, in which the molecules are reflected as if from a mirror. Though there is scope for argument about the speed of re-emission of the molecules in diffuse reflexion, the drag coefficients obtained under the various possible assumptions do not differ by more than about

Table 1. Values of Mass m and m/SC_D for Satellites 1957 α–1958 ζ

Satellite		Mass, m (kgm.)	m/SC_D (kgm./m.^{2})
Sputnik 1	1957 α 2	83	110
Sputnik 1 rocket	1957 α 1	—	62
Sputnik 2	1957 β	—	58
Explorer 1	1958 α	14	23
Vanguard 1	1958 β 2	1·5	23
Explorer 3	1958 γ	14	23
Sputnik 3	1958 δ 2	1,327	190
Sputnik 3 rocket	1958 δ 1	—	59
Explorer 4	1958 ε	17·5	29
Atlas	1958 ζ	3,960	28

5 per cent. It has been assumed here that the re-emission speed has a Maxwellian distribution about the speed appropriate to the temperature of the satellite, and drag from electrical forces has been ignored.

The value of SC_D is most difficult to estimate for the nearly cylindrical satellites, *Explorers* 1, 3 and 4 and *Atlas* (1958 α, γ, ε and ζ). It appears very probable, both on general dynamical principles and from observations[7], that each of these cylindrical satellites, and the rockets of the Russian satellites[10], have rotated about their axis of maximum moment of inertia, that is, an axis perpendicular to their length, though the angle between this axis of rotation and the direction of motion has varied. If this picture is correct, the two extreme modes of rotation are (*a*) travelling exactly like an aeroplane propeller, and (*b*) tumbling end-over-end. In (*a*), the axis of spin and the direction of motion are parallel; in (*b*), they are at right angles ; and in practice the angle may be anywhere between these extremes. A recent study (G. E. Cook, unpublished work) has shown that, under the assumption of diffuse reflexion, a rotating cylinder of length l and diameter d ($d \sim 0{\cdot}1\, l$) has a value of SC_D of about $2{\cdot}2\, ld$ under regime (*a*) and about $1{\cdot}5\, ld$ under regime (*b*). For any motion between these extremes, SC_D lies between $1{\cdot}5\, ld$ and $2{\cdot}2\, ld$. The nearly cylindrical satellites have been treated here as cylinders, with SC_D taken as $1{\cdot}85\, ld$, the mean of the values under regimes (*a*) and (*b*). If each satellite has rotated about its axis of maximum moment of inertia, this value of SC_D will not be in error by more than 19 per cent.

The spherical satellites *Sputnik* 1 and *Vanguard* 1 (1957 α 2 and 1958 β 2) both have cylindrical antennæ, and their drag coefficient C_D has been taken as 2·2, with S as the mean cross-section during one rotation. This value should not be in error by more than 5 per cent, since $C_D \simeq 2{\cdot}1$ for a sphere and $C_D \simeq 2{\cdot}2$ for a rotating cylinder. For the conical *Sputnik* 3 (1958 δ 2), S has been taken as the mean of the cross-sections in modes of rotation (*a*) and (*b*), with $C_D = 2{\cdot}3$. For *Sputnik* 2 (1957 β), no weights and dimensions are available, but the value of m/SC_D can be inferred from *Sputnik* 1. Since the perigee heights of *Sputniks* 1 and 2 were virtually the same[10], equation (2) gives :

$$\left(\frac{m}{SC_D}\right)_2 = \left(\frac{m}{SC_D}\right)_1 \sqrt{\frac{a_2 e_1}{a_1 e_2}} \left(\frac{dT}{dt}\right)_1 \Big/ \left(\frac{dT}{dt}\right)_2 \qquad (6)$$

where suffixes 1 and 2 refer to *Sputniks* 1 and 2, respectively. Since the factors on the right-hand side of (6) are known, $(m/SC_D)_2$ can be found. Values of m/SC_D for the rockets of *Sputniks* 1 and 3 (1957 α 1 and 1958 δ 1) can be found similarly. This indirect method should be reliable if, as is believed[16,17], each of the satellites 1957 α 1, 1957 β and 1958 δ 1 retained a virtually constant value of m/SC_D until the last day of its life.

The values of m/SC_D obtained by these various methods for the satellites with known orbits launched in 1957 and 1958 are listed in Table 1. If the assumptions already stated are justified, the error (standard deviation) in the tabulated values of m/SC_D will probably be about 10 per cent.

Evaluation of Air Density

If values of m/SC_D are available, the air density at height $0{\cdot}5H^*$ above perigee can be found from equation 5. For the Russian satellites, values of dT/dt, a and e have been taken from orbital determinations made in Britain[2,18–20]. For the American satellites, values have been obtained from the orbital data regularly issued as part of their prediction services by the Smithsonian Astrophysical Observatory, Cambridge, Mass., and Project Space Track, Bedford, Mass. The values of H^* chosen are consistent with values of H given later in this article.

The resulting values of density, from all the satellites in Table 1, are plotted in Fig. 2, and a curve has been drawn through the points to indicate likely average values for density. It is usual when constructing a 'model atmosphere' to make a plausible assumption about the variation of temperature and air composition with height, and thence derive density. Since the primary measurements are of density, however, it seems more logical to take the density as the basic parameter and then to deduce temperature from it. This procedure has the further merit that it shows the large errors in temperature which can arise, even when a good fit is achieved for the density.

Several features of Fig. 2 are worth noting :

(1) The ten different satellites give surprisingly consistent values of air density. None of the 15 plotted points in the cluster between 190 km. and 260 km. differs from the curve by a factor greater than 1·4, and the average factor of difference is about 1·2. Probably, therefore, the assumptions made were not grossly in error, as they would have been if, for example, one of the cylindrical satellites had flown like an arrow instead of rotating.

(2) Even if the method of analysis were perfectly accurate, the points in Fig. 2 would not all lie on the same curve, since the effective air density is known to vary from day to day and month to month, by up to 30 per cent at 200–250 km. height[16,17] and by a factor of 3 at 700 km. (ref. 21). The curve in Fig. 2 can therefore only represent average values.

(3) The points in Fig. 2 cover latitudes between 50° N. and 35° S. ; but there is no sign of any regular variation with latitude, and the spread of the points suggests that, between 50° N. and 35° S., density does not depart from its average value by a factor of more than about 1·5. This is in contrast with results from rocket experiments[22], which suggest a variation by a factor of up to 5 between 59° N. and 33° N. on a summer day. The accuracy of initial estimates of life-time for the Russian satellites, the perigees of which moved from an initial latitude near 50° N towards the equator, also suggests that density does not vary greatly within this range of latitude.

(4) The one point above 400 km. in Fig. 2 should not be taken seriously, partly because it is unsupported and partly because the effect of charged drag[23] is likely to be important at 700 km., where more than 5 per cent of the atoms may be ionized.

Table 2 lists values of average density from the curve in Fig. 2, for heights between 200 and 400 km., where the error-factor should not exceed 1·5.

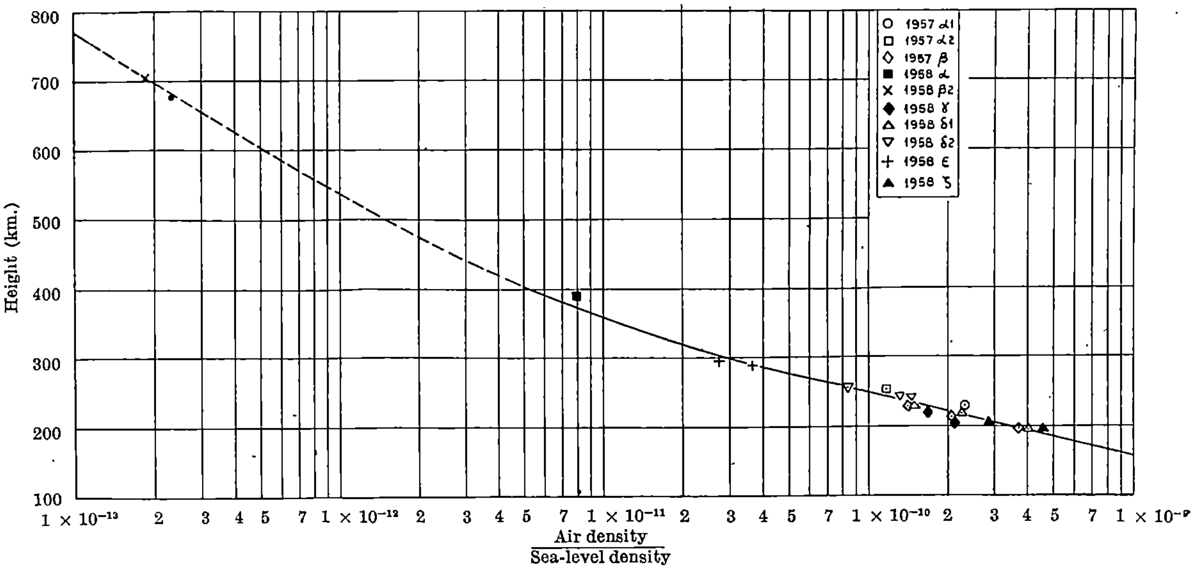

Fig. 2. Values of air density obtained from satellites 1957 α–1958 ζ, using equation 5

The air temperature should, in theory, be obtainable from the slope of the curve in Fig. 2; but in practice the accuracy is poor. Values of the coefficient H of equation 3 derived from the slope of the curve in Fig. 2 rise from $H = 37$ km. at 200 km. height to $H = 71$ km. at 400 km. height. But it is possible to link the points in Fig. 2 with other curves, of different slopes. For example, a straight line between 200 and 400 km. height, with $H = 50$ km., fits the points almost as well. There are other ways of finding H, the most direct being to use the equation connecting eccentricity e with perigee distance from the centre of the Earth, r_p. The appropriate expression for H, accurate to $\pm$ 5 per cent if $0{\cdot}015 < e < 0{\cdot}2$, is found (D. G. King-Hele and G. E. Cook, unpublished work) to be:

$$H = \frac{r_{p_0} - r_p}{\frac{1}{2}\ln\left\{\frac{ae}{a_0e_0}\left(\frac{8a_0e_0 - 3H}{8ae - 3H}\right)^2\right\} - \frac{a_0e_0 - ae}{a_0}} \qquad (7)$$

where zero suffix denotes initial values. This equation, like equation 2, is not significantly altered by the effect of the oblateness of the Earth. The value of H obtained from equation 7, using kinetheodolite observations of *Sputnik* 2, is $H \simeq 55$ km. at 200 km. height. It is, at present, difficult to choose between these rather scattered values of H. It seems probable however that, at heights between 200 and 400 km., the average value of H is near 50 km., and that H tends to increase with height. If a value had to be chosen, H might be assumed to rise from 45 km. at 200 km. height to 60 km. at 400 km. height, with an error-factor which should not exceed 1·5.

At heights between 200 and 400 km., the air temperature in degrees Kelvin may be expressed approximately as $1{\cdot}1\, MH/(1 - H')$, where M is the molecular weight of the air, H is in kilometres, and H' is the rate of change of H with height. The main constituents of the air at these heights are believed to be atomic oxygen and atomic nitrogen, in proportions as yet unknown[12,24–26]. If, then, M is taken as 15 and $H' \simeq 0{\cdot}07$, the average temperature between 200 and 400 km. height will be about 1,000° K. It should be emphasized, however, that any values of temperature are far less reliable than values of density.

I wish to thank Mrs. D. M. C. Walker for preparing the graphs in this article.

Table 2. Average Air Density at Heights between 200 km. and 400 km.

Height (km.)	Air density / Sea-level density	Density (gm./c.c.)
200	$3{\cdot}4 \times 10^{-10}$	$4{\cdot}1 \times 10^{-13}$
220	$2{\cdot}0 \times 10^{-10}$	$2{\cdot}5 \times 10^{-13}$
240	$1{\cdot}2 \times 10^{-10}$	$1{\cdot}5 \times 10^{-13}$
260	$7{\cdot}6 \times 10^{-11}$	$9{\cdot}3 \times 10^{-14}$
280	$4{\cdot}6 \times 10^{-11}$	$5{\cdot}6 \times 10^{-14}$
300	$2{\cdot}9 \times 10^{-11}$	$3{\cdot}6 \times 10^{-14}$
320	$2{\cdot}0 \times 10^{-11}$	$2{\cdot}4 \times 10^{-14}$
340	$1{\cdot}4 \times 10^{-11}$	$1{\cdot}7 \times 10^{-14}$
360	$9{\cdot}7 \times 10^{-12}$	$1{\cdot}2 \times 10^{-14}$
380	$7{\cdot}1 \times 10^{-12}$	$8{\cdot}7 \times 10^{-15}$
400	$5{\cdot}3 \times 10^{-12}$	$6{\cdot}5 \times 10^{-15}$

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OBITUARIES

Dr. W. R. G. Atkins, C.B.E., F.R.S.

The death occurred on April 4 of William Ringrose Gelston Atkins at the age of seventy-four. Son of the late Thomas Gelston Atkins, M.D., of Cork, W. R. G. Atkins was born on September 4, 1884. After his schooldays at the Friend's School, Newtown, Waterford, and the Grammar School, Cork, he went to Trinity College, Dublin, where he took two honours degrees in physics and chemistry, and in botany, zoology and geology. He was awarded Senior Moderatorships in Experimental and in Natural Sciences in 1906, and was then successively assistant, during 1906–11, to the late Prof. S. Young, the University professor of chemistry, and during 1911–20, to the late Prof. H. H. Dixon, the University professor of botany, in Trinity College, Dublin. The latter period was broken by the First World War, in which Atkins was an assistant chemist at Woolwich Arsenal in 1915 and a volunteer assistant in the Division for Aeronautical Chemistry of the National Physical Laboratory for the first six months of 1916. As a result of his work at the National Physical Laboratory, he was given a commission as equipment officer in the Royal Flying Corps to organize and direct a laboratory in the Experimental Aircraft Establishment at the Aboukir Depot in Egypt, reaching the rank of major in the Royal Flying Corps. After the War he went for a short time as indigo research botanist at the Imperial Department of Agriculture in India.

In 1921, Atkins was appointed head of the Department of General Physiology at the Plymouth Laboratory of the Marine Biological Association, where he remained until his retirement in 1955, apart from the years of the Second World War, when he served successively in the Home Guard, the Royal Army Medical Corps, and the Meteorological Office.

Atkins's research work thus falls into two distinct periods, that at Trinity College, Dublin, and that at Plymouth. During the first period it was mainly physico-chemical, including such subjects as the properties of urine and the osmotic pressures of blood and eggs of birds, and of plant tissues. While in Egypt he was specially concerned with the deterioration of fabrics and the study of lubricants. In 1916, he published a book entitled "Some Recent Researches in Plant Physiology".

On his arrival at Plymouth Atkins thus had a very wide background on which to draw for his new field of research, which was the physical and chemical conditions of sea water as an environment for marine life. During his long period at Plymouth he undertook researches, the results of which are now basic to all modern research on the productivity of the sea and have passed into essential background knowledge. These related chiefly to the seasonal variations in the chemical conditions, especially the nutrient salts, in sea water; and to the penetration of light into the sea and the effects of fine particles in suspension. In the latter field Atkins collaborated with Dr. H. H. Poole, of the Royal Dublin Society. As a side-line, Atkins continued work started in Egypt on the deterioration of fabrics, in this instance experimenting on methods of preservation of nets and ropes. His researches on chemical and physical conditions in the sea brought considerable fame to the Plymouth laboratory.

Atkins was an indefatigable research worker, and a noteworthy feature was the way in which he adapted his methods to many environments. For example, his chemical work on sea water was repeated on freshwaters and soils; and his measurements of light were made on land, in woods and in many parts of the world. For many years he ran a continuous light recorder on the roof of the Plymouth Laboratory. He also gave liberally of his advice in many spheres during the Second World War. The range of subjects on which he published is too wide to include in this brief notice.

Atkins held the degrees of M.A. and Sc.D., and was a Fellow of the Royal Institute of Chemistry and of the Institute of Physics; in the First World War he was twice mentioned in dispatches and was awarded the O.B.E. (Mil.) in 1919. He was elected a Fellow of the Royal Society in 1925, and in 1928 he received the Boyle Medal of the Royal Dublin Society. In 1951 he was appointed a Commander of the British Empire in the King's Birthday Honours. He was president of Section K (Botany) of the British Association for this year's meeting in York.

In his earlier days at Trinity College Atkins was an athlete, and besides playing hockey and rowing at Trinity College, he was especially noted for his boxing. He became middle-weight champion of Ireland.

A man of great integrity and kindness, he had very many friends from all parts of the world, to whom he and his wife extended much hospitality at their home at Antony in Cornwall. To Mrs. Atkins, and their married son, all who knew him will extend their sympathy. F. S. Russell

Prof. Erik Hägglund

Erik Hägglund died in Stockholm on March 13 at the age of seventy-one. His life was dedicated to the elucidation of the involved reactions in processing wood into cellulose and paper, more particularly the chemistry of the sulphite pulping process, its technology, and the nature of lignin and its secondary derivatives.

Hägglund obtained his scientific education at the University of Stockholm, being fortunate to come under the guidance of an inspiring teacher, Hans von Euler. He received his doctorate in 1914, presenting a thesis on the effect of *p*H on alcoholic fermentation. It is one of the very first critical investigations of modern type on hydrogen ion concentration. By the way, Hägglund was the first of von Euler's research students to become the incumbent of a university chair in chemistry among the twelve future professors who emerged from the Euler fold. Hägglund graduated three months before the outbreak of the First World War, during which research and chemical technology were given a potent impetus for the sake of national economy and feeding of the people. A few years earlier, the method of fermenting the sugars of waste liquor from the sulphite-pulping process had been worked out in Sweden, a method still used and of great importance in Scandinavia. Hägglund had already, in 1911, been investigating this problem at the University of Stockholm, collaborating with the inventors of this process. He was thus predestined for an industrial position. The step from the university to industry was then very unusual, in Sweden at least. However, Hägglund found his right field of work and contributed substantially to the ultimate success of the 'sulphite–alcohol' venture. The first and, even by now, the only scientific account of this interesting fermentation is given in his monograph, "Die Sulfitablauge und ihre Verarbeitung auf Alkohol" (1921).

It was quite logical for a man of Hägglund's acumen to inquire further into the problem of converting wood into alcohol—the hydrolysis of the main constituent of wood, the cellulose—to produce fermentable sugars. This difficult problem had already received a great deal of attention in many quarters, but in vain. The only technique of practical use existing is that developed by Hägglund and Bergius, the so-called Rheinau-method (1917) in which hydrochloric acid is used as hydrolysing agent.

The great ability of this young scientist in solving intricate technical problems by application of fundamentals was early recognized in academic circles. In 1920, Hägglund accepted the chair of the chemistry of wood products especially established for him at Åbo Akademi, the Swedish-language university of the new Republic of Finland. A flourishing school of cellulose research came into being, the research output became formidable and many of the fundamentals of the speciality established. Hägglund's work formed a continuation of that of the grand old man of lignin chemistry, Peter Klason, emeritus professor of chemical technology in the Royal Institute of Technology in Stockholm. Actually, Hägglund became the spiritual successor to Klason in 1930, when a chair in wood chemistry and technology was founded at the Royal Institute, through donations from the pulp and paper industries. Fourteen years later, the Swedish Government erected an institute for pulp and paper research, probably the largest and best equipped institute of its kind at that time, constituting a unit of the Royal Institute.

Hägglund and his many pupils—of whom quite a number occupy leading positions in this key-industry of Sweden at the present time—have, during the past twenty-five years, investigated practically every phase of the wood-pulping processes and paper making. Work of a fundamental theoretical nature as well as important contributions to technological aspects of this industry, which is, of course, of great importance for Sweden, have emanated from the Hägglund school. Among his numerous co-workers, Adler, Enkvist, Erdtman, Giertz and Johnson were prominent. It is generally conceded that Hägglund did more than any other single individual to unravel the intricacies of the 'cooking' processes—his research on the formation of lignosulphonic acids being particularly outstanding. His comprehensive text-books, "Holzchemie" (1928, 1939), "Natronzellstoff" (1926) and "The Chemistry of Wood" (1951), are standard works throughout the world.

His unflagging endeavour in furthering the progress and well-being of the industry to which Hägglund devoted his life gave him an international standing. He was a member of many learned societies at home and abroad and received several honorary degrees, that from the University of Heidelberg giving him great pleasure. Among numerous awards he received was the rare distinction of the Grand Gold Medal of the Royal Swedish Academy of Technical Sciences, and the greatest honour to be given a cellulose chemist, the Ekman and Mitscherlich Gold Medals.

Hägglund was a sterling character, an inspiring colleague and a staunch friend. He will be greatly missed by a large circle of friends and colleagues in many lands.

K. H. Gustavson

Prof. Alfred Kohn

Alfred Kohn, professor and director of the Department of Histology of the German University in Prague until 1937, died in Prague on January 15, five weeks before his ninety-second birthday. Born in Libin, Bohemia, he received his medical education at the German University in Prague and, while still a student, became assistant to the histologist, Siegmund Mayer, whom he later succeeded in the chair. For various periods in his career he was a senator of the University and dean of its medical faculty.

Kohn is famous for his work on the parathyroids, which he termed *Epithelkörperchen*. His contribution was to point out clearly their independence of the thyroid. He was, at least, a silent partner in Gudernatsch's discovery, made in Kohn's institute, that feeding thyroid to tadpoles inhibits their growth but accelerates metamorphosis. His best-known work deals with the paraganglia and the chromaffin system, which terms he introduced. There has been much dispute about the nature of paraganglionic cells, but recent electron microscopical investigations bear out his views. Kohn considered chromaffin cells to be a special category, comparable with epithelium, nerve cells, muscle cells and so forth. They form a link between nervous and endocrine systems. Kohn also made significant contributions to our knowledge of the differentiation of the peripheral nervous system, stressing the early differentiation of nerve cells ("*primogenitur*", *Hauptzellen*) and the later differentiation of Schwann cells, paraganglia and suprarenal medulla ("*secundogenitur*", *Nebenzellen*).

I worked with him for ten years, and in my view Kohn should be considered a great clarifier who put into focus many structures and problems then only vaguely known or misinterpreted.

During the Nazi occupation of Prague, it seems that some informal protection was first extended to him, but when a *Diener* of the German Anatomy Department saw Prof. Grosser, the well-known embryologist, talk to the Jew, Kohn, in the street, the seventy-four year old Kohn was deported to a concentration camp. He returned to Prague in 1945, but he met new difficulties: on account of his German education and his position in the abolished German University, he was deprived of his superannuation; however, following protest in the Czech Press, it was restored. Later, the Communist government bestowed on this entirely unpolitical scientist the Order of Labour, which carries a supplemental income, thus making comfortable the last years of his life. Max Watzka, who succeeded him in Prague and is now editor of the *Anatomische Anzeiger* and professor of histology in Mainz, is, of all Kohn's disciples, the one who continues most consistently the work of Alfred Kohn.

Rudolf Altschul

NEWS and VIEWS

The Royal Society : New Foreign Members

The following have been elected foreign members of the Royal Society : Prof. Melvin Calvin, University of California, Berkeley, California, distinguished for his researches into the mechanism of photosynthesis ; Prof. Gerhard Domagk, University of Münster, director of the Research Laboratories for Experimental Pathology and Bacteriology, Farbenfabriken Bayer, Wuppertal-Elberfeld, Germany, distinguished for his researches leading to the discovery of 'Prontosil', the first chemotherapeutic agent against septic infection ; Prof. Jan Hendrick Oort, State University of Leyden, The Netherlands, distinguished for his contributions to the knowledge of galactic structure, of stellar distribution and of stellar dynamics ; Prof. Axel Hugo Teodor Theorell, of the Nobel Medical Institute, Stockholm, Sweden, distinguished for his work in the field of enzyme chemistry, particularly in relation to oxidation in animal tissues.

Overseas Geological Surveys :
Dr. Frank Dixey, C.M.G., O.B.E., F.R.S.

Dr. Frank Dixey will retire on June 30 from the post of director of Overseas Geological Surveys. Dr. Dixey graduated in the University of Wales in 1914. After service on the Western Front from 1915 to 1918 he was appointed government geologist in Sierra Leone. He worked in Africa for nearly thirty years, and was successively director of the Geological Survey of Nyasaland (1921–39) ; director of Water Development, Northern Rhodesia (1939–44) ; and director of the Geological Survey of Nigeria (1944–47). In addition, at various times in the years 1938–44, he carried out advisory work on water development and on geological survey matters for the Governments of the Sudan, Eritrea, Kenya and Tanganyika. In 1947 the Directorate of Colonial Geological Surveys was inaugurated as a central organization in London to link and provide specialist services for the surveys overseas, and Dr. Dixey became its first director. There were then eleven Colonial territories with Geological Survey Departments. In the next ten years surveys of thirteen other territories were organized ; the number of senior staff overseas was increased from 50 to 212 ; Photogeological and Geophysical Sections were set up in London ; the Mineral Resources Division was formed by transfer from the Imperial Institute, and its activities were extended ; and among many other developments, arrangements were made for extensive co-operation with universities and other institutions in the United Kingdom. The establishment of this thriving organization is the climax of an official career during which Dr. Dixey has been the author of more than 130 publications, relating mainly to Africa. Their range includes mineral resources and water supply, Karroo and Mesozoic stratigraphy, the rift system, many aspects of geomorphology, and petrological topics, including work in collaboration with Dr. W. Campbell Smith and Mr. C. B. Bisset which afforded the first recognition of carbonatites in Africa. Dr. Dixey was awarded the Draper Medal of the Geological Society of South Africa in 1945, and the Murchison Medal of the Geological Society of London in 1953. Since 1948 he has been president of the Association of African Geological Surveys.

Dr. S. H. Shaw, O.B.E.

Dr. S. H. Shaw has been appointed to succeed Dr. Frank Dixey as director of Overseas Geological Surveys. Dr. Shaw, who is fifty-five, graduated in 1926 at the Royal School of Mines with first-class honours in mining and mining geology. From 1926 to 1928 he worked with the late Dr. A. Broughton-Edge on electrical prospecting in what is now the copper-belt in Northern Rhodesia, and from 1928 to 1930 in Australia as a member of the Imperial Geophysical Experimental Survey. He then returned to the Royal School of Mines as a demonstrator in the Experimental Department. In 1932 he joined the staff of the Geological Department of the University of Birmingham, where he continued his work on the development and application of various methods of geophysical prospecting, including resistivity measurements in boreholes. At the invitation of the Government of Southern Rhodesia, he visited that country in 1933 to make tests of resistivity methods for locating underground water supplies, with results which led to the adoption of these methods as standard procedure. In 1937 Dr. Shaw was appointed as government geologist in Palestine, where he served until the termination of the mandate in 1948. In 1949 he joined the Directorate of Colonial Geological Surveys, and was charged with the task of initiating and developing the Photogeological and Geophysical Sections. He was promoted to deputy director in 1950. Dr. Shaw's publications include part-authorship of the official report of the Imperial Geophysical Experimental Survey, and a series of papers on resistivity work and on the estimation of free quartz in rocks by micrometric methods.

Geology at Leicester :
Prof. P. C. Sylvester-Bradley

Peter Colley Sylvester-Bradley, appointed to the recently created chair of geology in the University of Leicester, was educated at Haileybury and the University of Reading. After a short period in charge of the Department of Geology at the Seale-Hayne Agricultural College (1937–39) he served in combined operations, and later as administrative officer in a branch of the Admiralty Operations Division in the Mediterranean. His appointment to the staff of the Geology Department of the University of Sheffield followed in 1945, and there he now holds the post of senior lecturer in geology.

Bradley's comprehensive teaching experience also includes an appointment as visiting Rose Morgan professor in the University of Kansas during 1955–56. His researches in palæontology have dealt authoritatively with fossil Ostracoda, for he is part author and general co-ordinator of the volume dealing with these fossils in the "Treatise on Invertebrate Palæontology". Other fields of palæontological research are concerned with the fossil oysters of the Jurassic of north-west Europe, and with the ammonites of the Lias of the Yorkshire coast. His published work also bears witness to a deep interest in fundamental and philosophical aspects of palæontology, such as those concerned with the study of communities, with speciation, and with the taxonomic problems which arise therefrom. This varied and successful research activity has been recognized by the Geological

Society of London in the awards of the Wollaston Fund in 1953, and the Edmund Johnston Garwood Fund in 1957.

Bradley's active participation as a member of council of a number of geological societies and associations, together with a period (1953–57) as editor of the Yorkshire Geological Society, is a measure of the importance of his contribution to, and interest in, the welfare of his science. His enthusiasm and energy are combined with a strong and pleasant personality and his friends and colleagues look forward with anticipation to a most successful tenure of the chair of geology at the University of Leicester.

Ministry of Supply :
Mr. Lewis Boddington, C.B.E.

Mr. L. Boddington, a deputy chief scientific officer and director of Royal Naval Aircraft Research and Development at the Ministry of Supply, has been appointed to the rank of chief scientific officer, and will become the director-general of Aircraft Research and Development (R.A.F.) ; he succeeds Air Vice-Marshal P. S. Blockey, whose tour of duty with the Ministry of Supply expires in July. Mr. Boddington has been associated with research and development on naval aircraft and aircraft-carrier equipment during the greater part of his career. He joined the Royal Aircraft Establishment in 1936 and became superintendent of the Design Department in 1944. From 1946 until 1951 he was superintendent of the Naval Aircraft Department ; he was appointed to Ministry of Supply headquarters in 1951, and later became the director responsible for naval aircraft research and development. He has become recognized internationally as the leading authority on naval aeronautics, and his name has been associated with a number of important developments in this field. In particular, the angled deck, of which he was the joint inventor, and the mirror deck-landing sight, which was developed under his direction, have made the operation of aircraft from carriers very much easier and safer, and have been adopted by both the Royal Navy and the United States Navy. He has also been responsible for the planning and direction of the Royal Aircraft Establishment's new research facilities for naval aircraft at Bedford. In recognition of his services to the development of naval aircraft he was awarded the Bronze Medal of the Royal Aeronautical Society in 1953.

Science Correspondent of the B.B.C.: Mr. C. L. Boltz

The British Broadcasting Corporation has created a new post at Broadcasting House, that of science correspondent in the News Division. The post is comparable to that of the Division's diplomatic and industrial correspondents and will involve duties on both sound and television. Mr. C. L. Boltz has been appointed to the post. He joined the B.B.C. in 1952, as science correspondent on the European Service, and has been broadcasting to Europe ever since. Educated at Huish's School, Taunton, and at University College, Exeter, Mr. Boltz graduated in mathematics and physics, later taking a degree in psychology at Birkbeck College (University of London) with a view to research. After a period spent in research and teaching (during the War he taught radar at Hackney Technical College), he turned to science writing. Among his best-known books are "Wireless for Beginners" and "A Statue to Mr. Trattles". He has contributed to a number of scientific journals, including *Nature* and *Discovery*. He has been an active Fellow of the Physical Society for fifteen years and has served on the Colour Group's committee for two periods. Few people have had so wide an experience of science broadcasting, for during the time he has been broadcasting from Bush House he has covered a vast range of scientific topics. Among European listeners he has a great reputation and he is one of the most popular broadcasters to give talks at Bush House.

International Commission on Higher Education in Nigeria

It was announced on April 27 that the Nigerian Government has invited a Commission comprising Nigerian, American, and British members to investigate Nigeria's needs in post-secondary education over the next twenty years, and to recommend to the Nigerian Government what steps should be taken to meet these needs. The cost of this operation is to be met by a grant from the Carnegie Corporation of New York. Sir Eric Ashby, Master of Clare College, Cambridge, has accepted an invitation to be chairman of the Commission. The names of other members of the Commission will be announced when they have all accepted invitations. It is proposed that the full Commission should meet in Nigeria in January and again in August 1960, and should produce a preliminary report for the Nigerian Government by October 1960, when Nigeria attains full independence.

Intelligence Unit for Natural History

The formation last year of the Council for Nature (*Nature*, 181, 867 ; 1958) has given cohesion to the natural history movement in Great Britain, but there is a fundamental need for a central information service on matters concerned with natural history and nature conservation. At present there is no authoritative source of up-to-date information on these subjects available to naturalists. The B.B.C. has agreed to make an annual grant of £5,000 for three years to enable the Council for Nature to establish an Intelligence Unit, the first task of which will be the collection of information on what work is at present being undertaken by individual naturalists and by societies and various other bodies. By the end of the year it should be possible for the Council to provide information and advice, and to foster co-operation schemes of work and intimate what is required in the investigations of neglected fields of work. In particular it is hoped that help and encouragement can be given to amateur cinematographers wishing to make nature films. These are very important in fostering an interest in wild life in a population which is becoming increasingly urban. The Council for Nature (41 Queen's Gate, London, S.W.7) is grateful to the B.B.C. for its support, which is unconditional and places no restraint on the general services to all.

Space Research in Britain

In replying to a question in the House of Commons on April 20, the Minister of Supply, Mr. A. Jones, said that the United Kingdom missile programme could, with some adaptation, give an initial launcher in aid of a space research programme, but of itself could provide neither the satellites nor the instruments needed to attack the scientific problems of space research. The Government was at present considering the question of a British space research project using Earth satellites in the light of advice from the

Advisory Council on Scientific Policy. The Government had in mind the scope such a project would provide for co-operation with Commonwealth countries, but such discussions could most profitably proceed when the scale and nature of any British effort had been decided. Mr. Jones agreed that the danger of losing our youngest and ablest scientists to the United States in the absence of occasional opportunities for such research, even if it involved using equipment originally designed for a specific military purpose, was an important consideration. Mr. Jones promised that a statement would be made quite soon.

Commercial Manufacture of Nuclear Fuel Elements

In reply to a question regarding the circumstances in which a private company was permitted to manufacture nuclear fuel elements, and the security reasons for the refusal of the Parliamentary Secretary to the Ministry of Power to reveal, on April 21, which organization other than the Atomic Energy Authority was preparing to make such elements, the Prime Minister stated that the Parliamentary Secretary was unwilling to go into greater detail until he had been able to refer to the defence authorities as to whether any question of security arose. Mr. Macmillan now saw no objection to stating that it was the intention that Rolls-Royce, Ltd., should manufacture fuel elements for nuclear submarine machinery. The material would be supplied by and would remain the property of the Admiralty. At present all nuclear fuel was manufactured by the Authority, but it was likely that in future elements would be manufactured in some of the processes of industry. The Nuclear Installations (Licensing and Insurance) Bill at present under consideration in Committee ought to provide for this, and all such material would either be the property of the Authority or manufactured only under licence and control, for which the Bill set up a proper system. Except for a certain amount of processing, Mr. Macmillan thought that for many years all nuclear fuel would be supplied either by the Atomic Energy Authority or, for defence purposes, by the Defence Departments.

The Royal College of Surgeons of England

The recent intense activity in the Royal College of Surgeons, which has aroused considerable interest among both the professional and lay public, is not in fact a recent development. Before the Second World War the scientific work undertaken by the College had been extended by adding a Department of Physiology to the old-established Departments of Anatomy and Pathology in Lincoln's Inn Fields, London, and by establishing a centre for experimental surgical research, the Buckston-Browne Farm, at a site adjacent to Darwin's old home at Downe. But since the War, the programme of research and education has gained fresh impetus from the need for reconstruction after the grievous damage which the College suffered in 1941, and from the needs of postgraduates seeking higher qualifications in surgery, dental surgery and anæsthetics. When planning the rebuilding of the College, the Council therefore resolved that laboratories should take the place of some of the destroyed museums, and that Departments of Pharmacology and Biochemistry should be established to provide a complete syllabus of postgraduate education in the basic medical sciences which would be available not only to young surgeons but also to all postgraduates studying for any of the higher diplomas for which these subjects are required. Recognizing that teachers must be provided with accommodation and equipment for research if a high academic standard is to be maintained, the College included in its building programme a very considerable expansion of the floor area for laboratories as well as a corresponding extension of the Library. These plans were designed to discharge what the Council regarded as its plain duty to postgraduates, and to meet its ancient obligation to promote the science as well as the art of surgery.

In making these decisions the Council had to face the problem of finding the money to pay for new buildings and to maintain the new research departments. Fees from students and the welcome contribution from the University of London through the British Postgraduate Medical Federation provided only a small fraction of the sums required, which now stand at £350,000 to complete the buildings and an annual £150,000 for the salaries of teachers, research workers and technicians and for laboratory maintenance. The College exerts a far-reaching influence upon the National Health Service, but is not a hospital and therefore is not eligible for a direct grant from the Government. The Fellows have contributed handsomely to College funds, thus showing their confidence in the policy of the Council; but in order to raise these large sums of money an appeal to the public for funds has recently been launched. Already most generous support has been forthcoming from the friends of the College in industry, commerce and in the world of finance, whose example should be followed by many others who have the understanding and the vision to see that by supporting surgical research and education they are promoting the best interests of themselves, their families and their dependants.

Italian Nuclear Research Centre at Ispra

The President of Italy, Signor Gronchi, formally opened the Italian Nuclear Research Centre at Ispra on April 13 before a distinguished gathering of about a thousand people. Ispra is about a mile from the extreme south of Lake Maggiore and about 35 miles from Milan, with which it is connected by *autostrada*. The centre is set in a beautiful district and occupies 340 acres of part grassland and part woods. Ultimately it should have a working population of around a thousand. Work began on the site in the late summer of 1957 and later in the year an organization headed by Prof. Carlo Salvetti was set up in Milan to prepare for the move to Ispra. About three weeks before the official opening of the centre, *Ispra*-1, a 5-MW. heavy water-moderated research reactor, fueled by 20 per cent enriched uranium with a fast neutron flux of $1 \cdot 1 \times 10^{14}$ n/cm.^{2} sec. and a thermal neutron flux of 8×10^{13} n/cm.^{2} sec., went critical. This reactor is a modification of the *CP*-5 reactor at the Argonne National Laboratory which operates at 1 MW. The moderator and fuel for the reactor were imported from the United States, as were some of the most important reactor components, so as to speed up the construction of the reactor. At the opening ceremony the United States Atomic Energy Commissioner, Mr. Floberg, made a speech in Italian and handed a cheque for 350,000 dollars to President Gronchi as the American contribution to the cost of the reactor.

Ispra-1 is enclosed in a gas-tight metal cylinder, 79 ft. high, which is kept at a negative pressure as a safety measure. Several laboratories are grouped around the reactor, and a metal chimney stack, more than 200 ft. high, towers over the metal shell. The reactor is intended primarily for research purposes and its scope of activities is very similar to that of the *Pluto*-type reactors, to which it bears some resemblance. The Ispra centre will provide a valuable addition to the Italian nuclear scene, which includes the centre for fundamental research at Frascati and the new centre for research studies to be built near Rome. Italy, in common with most countries in western Europe, is increasing its consumption of power at the rate of about 7 per cent a year, and with the hydroelectric power potential in the north fully exploited, Italy has begun a nuclear power programme that should give a capacity of 500 MW. by 1964. At present the 200-MW. reactor being built by the Nuclear Power Plant Company for Agip Nucleare is the most advanced of the reactors under construction.

Braille Translation by Computer

IBM MATHEMATICIANS, working with the American Printing House for the Blind, have developed a process for translating printed text into Braille by computer. The computer used is an *IBM* 704 which can convert a 300-page book into Braille in an hour—a job that would take skilled translators more than six days. This new technique will make available many school and technical books now rarely produced in Braille, thus enlarging the possibilities for careers for the blind. To speed this translation, printed texts will be recorded on magnetic tape and distributed to IBM computer installations, where they will be translated and the cost borne by IBM United Kingdom, Ltd.

Writing Braille requires knowledge of many complicated rules, the symbols often changing their meaning in a different context. Braille consists of 63 combinations of six raised dots which represent not only the letters of the alphabet, numerals and punctuation marks, but also 183 special contractions and abbreviations, as in the case of shorthand. Texts to be translated by the computer are first transcribed on to punched cards. The cards are then fed directly into the computer, which has had previously stored in its memory a programme for conversion of English into Braille. The translated text emerges from the computer in coded symbols on punched cards, and these, in turn, are fed to the printer unit of the *IBM* 704, which reproduces Braille symbols above the English text. After editing, the corrected punched cards are fed into an embossing machine which produces metal plates ready for use on a rotary press.

Denudation and Burial of Archæological Structures

THE British Association (Section *H*) has formed a special committee to "investigate by experiment the denudation and burial of archæological structures". The aim of the committee, the members of which are Dr. G. W. Dimbleby (chairman), Dr. P. Jewell (secretary), Prof. R. J. C. Atkinson, Dr. I. W. Cornwall and Dr. B. Proudfoot, is to obtain precise measurements of the rates at which soil moves and accumulates, how far buried objects may move in the soil, and the way in which buried objects disintegrate and decay. Building a simple ditch and bank with incorporated markers, and following the rate of silting of the ditch, and of denudation and spreading of the bank, formation of turf and compaction of soil, over the following years would help to answer some of the questions. Comparative results will be obtained from sites established in different parts of Britain. The observations should not only aid in the interpretation of archæological excavations but may throw more light on the changes that past land-use has produced. Buried materials will include wood, charcoal, bone and metal, treated in different ways, and their examination in the future may enable more information to be obtained from the accumulating finds from archæological sites. The committee will be very glad to hear from anyone interested in the project, particularly those whose specialist knowledge might help in laying out the structures, and who in turn might derive information of interest from the experiments. The secretary of the committee is Dr. P. A. Jewell, Royal Veterinary College, London, N.W.1.

A Century of Biological Research in Illinois

THE Illinois Natural History Survey Bulletin (27; 1958), entitled "A Century of Biological Research" (Pp. vi+85–234. Urbana: Illinois Natural History Survey, 1958), deals with the development of biological research in a mainly agricultural community, in which the practical problems affecting land-use and agriculture have largely controlled the outlook of the investigators as well as the policy controlling development. This is reflected in the five main lines of progress summarized, namely, economic entomology, faunistic surveys, applied botany and plant pathology, aquatic biology, and wild-life conservation. The work has, however, included notable contributions of a fundamental nature, and the brief outlines of these included in this Bulletin are of considerable interest. The rapid changes in Illinois due to the transformation of woodland and swamp to farmland, and to the utilization of the now 'vanishing prairies', have all greatly affected the plant and animal populations. These have been followed in studies and records which can scarcely be paralleled anywhere over so long a period. As one example, map records are given of the density of populations of a wheat predator, the chinch bug (*Blissus leucopteris*), available since 1840. Other examples trace the gradual disappearance of prairie animals, such as the prairie chicken, as arable land has replaced grassland, while the recorded fluctuations of the bob-white quail or of ducks and geese or of introduced pheasants, in areas of diverse ecological character, have abundantly justified the bird-census techniques which were adopted at an early date. Very well known to fresh-water biologists are the massive pioneer papers on the plankton, bottom-fauna and fishes of the Illinois River. Not only do they record some of the earliest quantitative work in these fields but also the 'indicator' species present and succeeding one another, as drainage and pollution modified the character of the river. This Bulletin is therefore a valuable guide to records which trace the growth of modern aspects of wild-life conservation from earlier efforts concerned simply with crop protection. It is, incidentally, also a memorial to the genius and foresight of A. S. Forbes, who for so long guided the destinies of the organization.

National Science Foundation Fellowships

THE National Science Foundation has awarded 1,100 graduate fellowships in the natural sciences and allied fields for the academic year 1959–1960. In addition, the Foundation has announced the names of 160 winners of regular postdoctoral fellowships. Of the graduate awards, 216 were made in the life sciences, 866 in the physical sciences, including a number in interdisciplinary fields, and 18 awards were made in certain areas of the social sciences. Of the postdoctoral awards, 55 were made in the life sciences, and 104 in the physical sciences, including a number in interdisciplinary fields, and in the field of econometrics.

The Genetic Concept of the Origin of Cancer

THE theory that malignant transformation in cells may be considered to be a genetic event was suggested in 1908 by J. A. Murray of the Imperial Cancer Research Fund (London), but experimental evidence had to wait twenty-years until inbred mice were available. In this respect the credit is due to the pioneering work of Dr. L. C. Strong (Buffalo), who was the organizer and chairman of a conference on "The Genetic Concept for the Origin of Cancer", supported by the New York Academy of Science and the National Institutes of Health (Bethesda). The papers presented by 29 contributors at the Conference, which was held in New York, October 1957, have now been published (*Ann. N.Y. Acad. Sci.*, 71; 801–1241; 1958). They are representative of the various aspects of cancer research of the past three decades. The diverse subjects discussed include: the role of genetic and environmental influence in the causation of experimental cancer; the effect of selection on transplanted tumours; the occurrence of tumours in plant and animal interspecific hybrids; the modifying effects of genes on melanotic tumours in the fruit fly *Drosophila*; the nature of carcinogen-induced mutations in *Neurospora*.

J. Schultz (Philadelphia) attempted to show how our knowledge of genetical changes in somatic cells can be related to malignant change. D. B. Amos (Buffalo), on the other hand, gave examples to illustrate how the antigenic patterns of tumours can be used as a tool to study somatic genetics. The relationship between chromosome changes in tissue culture of mammalian cells and those observed in tumour cells was brought to the fore by A. Levan (Lund) and J. J. Biesele (New York); the possible relevance of certain types of phage mutations to malignant transformation of cells was discussed by S. E. Luria (Urbana). Papers by P. A. Gorer (London) and C. P. Oliver (Austin) deal with the genetics of human cancer, both agreeing that genetically determined predisposition to a particular type of cancer is present in certain families.

Royal Institute of Chemistry: Officers

MR. E. LE Q. HERBERT, managing director of Shell Refining Co., Ltd., was recently elected president of the Royal Institute of Chemistry for 1959–61. He took over this office from Dr. D. W. Kent-Jones (president 1955–57), who had been acting president since the death, on December 19, 1958, of Prof. W. Wardlaw (elected president for 1957–59). Dr. C. W. Herd, Prof. Charles Kemball and Mr. Clifford Paine were elected vice-presidents for 1959–61. Prof. Harold Burton was re-elected honorary treasurer for the ensuing year.

Iron and Steel Institute: Changes on Council

The following new members were recently elected to the Council of the Iron and Steel Institute: *President*, Mr. W. Barr; *Honorary Treasurer*, Sir Julian Pode; *Vice-Presidents*, Mr. B. Chetwynd Talbot (chairman and managing director, South Durham Steel and Iron Co., Ltd.), Mr. C. H. T. Williams (managing director, Park Gate Iron and Steel Co., Ltd.); *Ordinary Members of Council*, Major W. R. Brown (chairman, Ashmore, Benson, Pease and Co., Ltd.), Mr. T. R. Craig (director, Colvilles, Ltd.); *Additional Honorary Members of Council*, Dr. N. P. Allen (director, Metallurgy Division, National Physical Laboratory), Mr. A. Jackson (technical adviser on steelmaking, United Steel Companies, Ltd.).

Announcements

DR. D. A. LONG, recently on the staff of the Medical Research Council at the National Institute for Medical Research and during 1957–58 visiting professor in microbiology in the School of Medicine at the University of Pittsburg, has been appointed chief medical adviser and head of the Medical Research Department of the Wellcome Foundation, Ltd.

THE Physical Society is holding a conference on "Co-operative Phenomena and Phase Transitions" at King's College, Newcastle upon Tyne, during July 6–7. Further information can be obtained from the Secretary, Physical Society, 1 Lowther Gardens, London, S.W.7.

UNESCO is holding an arid zone symposium at the Instituto Nacional de Investigaciones Agronomicas, Madrid, during September 24–30. Summaries of proposed papers must reach the Department of Natural Sciences, Unesco, Place Fontenoy, Paris VII, by June 1. Further information can be obtained from the above address.

A CONVENTION on "Television Engineering in Science, Industry and Broadcasting", organized by the British Institution of Radio Engineers, will be held in the University of Cambridge during July 1–5. Delegates may reside in the colleges of the University. Further details can be obtained from the Secretary, British Institution of Radio Engineers, 9 Bedford Square, London, W.C.1.

AT the summer conference of the Society for Applied Bacteriology, to be held in London during July 7–9, a symposium will be held on "Lactobacilli". Those interested in attending, or contributing to, this symposium can obtain further details from the honorary secretary, G. Sykes, Boots Pure Drug Co., Ltd., Microbiology Division, Standards Department, Nottingham.

THE fourteenth Annual Electronics Exhibition and Convention of the Northern Division of the Institution of Electronics will be held at the Manchester College of Science and Technology during July 9–15. It will include extensive displays of electronic equipment of interest in all branches of science and industry. Details can be obtained from the Honorary Exhibition Organizer, Mr. W. Birtwistle, 78 Shaw Road, Rochdale, Lancs.

A MATHEMATICAL colloquium is to be held under the auspices of the Edinburgh Mathematical Society in University Hall, St. Andrews, during July 8–18. The principal speakers will be: Prof. H. S. M. Coxeter (subject to be announced), Prof. V. C. A. Ferraro (magnetohydrodynamics), Prof. C. Lanczos (linear operators and function spaces), Dr. A. P. Robertson (functional analysis), and Dr. R. Schlapp (history of mathematics). Further particulars and forms of application can be obtained from Mr. J. R. Gray, St. Salvator's College, St. Andrews.

EDUCATION FOR GOVERNMENT

A DEBATE on the motion "That the education of our future rulers should be primarily in the sciences rather than the humanities" was held in the Beveridge Hall, Senate House, University of London, on March 18. Sir Cyril Hinshelwood was in the chair; the motion was proposed by Sir Alexander Fleck, seconded by Prof. A. R. Ubbelohde, and opposed by Prof. B. Farrington, seconded by Prof. W. Beare. The debate was sponsored jointly by the London Section of the Royal Institute of Chemistry, the London branch of the Classical Association and the Haldane Society.

Sir Cyril remarked, in opening the proceedings, that he supposed he owed his position on the fence on this occasion to the fact that he happened to be president of the Classical Association as well as president of the Royal Society. He asked that there should be a straight fight on the arts versus science issue implied in the motion, but in this he must have been rather disappointed. Scarcely a speaker could be found to defend the motion as worded, and it was necessary even for Sir Alexander Fleck to assure his audience that whatever he might say, he was, in fact, moving the motion. His reluctance to do so stemmed not only from his slender acquaintance with the classics—failures in Latin having on two occasions "almost wrecked an otherwise promising career"—but from his dislike of the term "our future rulers". Any suggestion of a Platonic *élite*, selected by some process of intellectual eugenics, was repugnant to him. But there was an urgent need to orient the education of the people as a whole so that the statesmen and leaders they produced would be capable of handling scientific ideas. He contrasted, not too seriously, the legendary pedantry and other-worldliness of the classical scholar, with the severely practical, positive approach which a scientific training could bring to the consideration of human affairs. He believed, with Lord Cherwell, that it was more important to know something of the properties of chlorine than of the improprieties of Clodius. The continued growth of science and of informed opinion about science was vital to our country and to all peoples.

Prof. Benjamin Farrington, in a persuasive speech, opposed the motion on the grounds that it appeared to imply that there should be a compulsory tilt in the whole educational system so as to give primary emphasis to science. He had no quarrel with science—we should spend even more of our resources upon it in the future than we do at present—but it was essential that science remained the servant, not the master. The transformation of human life by science in the past three hundred years had been remarkable, but it had produced problems to which science by itself had no answers. The problems raised by automation, for example, or the whole question of man's survival, were beyond purely scientific answers. The humanist could survey the whole development of the marvellous being we called Man. This did not imply a backward-looking philosophy: it was the only hopeful way of looking to the future. Man alone had the power of creating his own inner world, the world of ideas, and he had drastically changed life on earth by his rational acts. The human intellect was the greatest force in the universe, since it alone could produce change. Science was one of man's achievements, but it was not the only one of significance. Scientists often seemed excitable, unstable, and at the mercy of every new idea. They were apt to be misled into new superstitions and to confuse their abstractions and concepts with reality. Hence one heard of discussions about the psychology of the man-made machine, when no machine could possess consciousness. The study of conditioned reflexes in organisms was important, but they did not supersede the rational acquisition of knowledge. The humanist was concerned with the conscience of man, in which is enshrined all the long history of man's endeavour; he must remain master.

Prof. A. R. Ubbelohde was prevented from being present by illness and his speech in support of the motion was read for him. The role of science had changed completely since the time when Dr. Johnson had ruled that "speculations upon matter are voluntary, and at leisure". It was necessary to continue the age-old process of adapting the content of education to the requirements of a changing society and admit science to the priority. A knowledge of science should be as fundamental an element of education in the future as were reading, writing and arithmetic to-day. Our future leaders would be at a disadvantage if they had not had scientific training; to understand and control the power of science would be one of their prime responsibilities. We could not risk that the potentialities of applied science should be at the mercy of "humanistic Druids" whose sympathies lay wholly outside the sciences. Scientific knowledge now formed one of the major empires of the human intellect; its disciplines threw new light upon old problems of human existence. The scientist soon learnt a humility in the face of objective facts which would stand many a politician in good stead. He was also accustomed to co-operating with his fellows across national boundaries in an international community of endeavour. There were dangers in too narrow an approach in scientific studies, as there were in all academic studies, but these were recognized and could be avoided. It would be a far greater danger to leave our future rulers in ignorance of science.

Prof. W. Beare, in seconding the opposition, said that the fact that they were debating this motion showed that there was a widespread uneasiness about the objects of education. Since there was no clear answer it was important to preserve freedom of choice. The idea that the education of the whole community should be compulsorily slanted was dangerous. It were better that a man should be a first-rate historian than a second-rate chemist. Our citizens and voters would be better guided by a knowledge of history than of quantitative science, but the study of any subject could not, of itself, make a good citizen or ruler—it was the knock-about of everyday life which was the true education. He did not grudge the scientists their palatial new premises, even though a new hat-rack might prove to be more than could be managed for the arts faculty. But a knowledge of thermodynamics would tell you nothing about hell-fire; our rulers should come from the humanists who had studied the imperfections and sins of man, as well as his potentialities.

When the discussion was thrown open it soon became clear that the motion had found few friends. The first two speakers were classicists; Dr. R. E. Witt spoke from experience as a headmaster of a grammar school and said that the study of Greek seemed to produce a greater humility, a greater readiness to look on the other side of a problem, than the study of scientific subjects. Mrs. M. Lockwood suggested that our leaders should have a humanistic philosophy within which their problems could be judged. Scientific progress seemed frighteningly aimless and uncontrolled; there was a suspicion that the real spur to our scientific effort was simply fear of the U.S.S.R. Prof. Timonen, of the University of Helsinki, pointed out that some of the greatest scientists had had a sound classical education and that this had probably contributed to their clarity of thought and expression.

There followed contributions by four chemists, but only one favoured the motion. Dr. A. C. C. Newman urged the importance of inculcating moral values during the education of the citizen. Political leaders had to deal with issues which were primarily moral and human; so long as they were well advised on scientific questions that was enough. Dr. H. J. Barber suggested that the study of the history of science could provide a valuable synthesis of the humanities and the sciences; it should take its place in curricula along with political history. Mr. R. A. Frazer disliked the suggestion that the sciences should predominate in education—a balance should be struck with emphasis primarily on the humanities. Mr. F. F. Ross agreed that the learning of Latin was a valuable discipline in primary education, but it should give way to science later. An understanding of man's scientific progress was basic to the study of history.

Prof. Farrington, in replying for the opposition, deplored the fact that the necessary expansion of the science faculties of British universities had been accompanied by drastic reductions in the facilities for studying ancient and modern languages and cultures. This was bringing about an undesirable change in the character of the universities themselves.

Sir Alexander Fleck, summing up for the motion, strenuously denied that the motives for the expansion of science were political. Man might not live by bread alone, but bread was still a necessity, and it was up to science to provide it. Only if our leaders understood science could it be used to improve life on earth.

Sir Cyril Hinshelwood then put the motion to the meeting and it was heavily defeated. A vote of thanks to the chairman and the speakers, proposed by Dr. S. A. Miller, was carried with acclamation.

N. LINDOP

DETERGENTS, TEXTILES AND DYES

A CONFERENCE on "Detergents, Textiles and Colour", organized by the Textile Institute in collaboration with the Branded Textiles Group, was held on February 11 in the Lesser Free Trade Hall, Manchester. Mr. Roland Thomas (director, C.P.A., Ltd., Branded Textiles Group), opening the meeting, said that the products produced by the Group were guaranteed and that members of the Group were interested in maintaining high quality in a very large range of textile goods. Serious consideration had been given for two and a half years to problems arising from the new detergents; on the subject of deterioration of textiles, the detergent manufacturers' attitude to complaints had been that: (*a*) they were not true, (*b*) if true, it did not matter, (*c*) if it did matter, nothing could be done about it, and (*d*) if anything could be done, it would be too expensive. The problem was serious, the housewife was lost in the complexities of advertisements and it was the business of industry to find a solution.

In the morning three papers were read and a number of excellent demonstrations shown to illustrate loss of tint by lack of fastness of dyes to detergent mixtures, by contamination by fluorescent bleaches and by chemical bleaching.

Mr. C. F. Ward (on behalf of the Branded Textiles Group) referred to the great increase in recent years in the number and variety of textiles and also of detergents and substances added to the synthetic soaps. It was fortunate, he said, that in this change emphasis has been placed by the textile manufacturer more and more upon quality. He listed detergent requirements and mentioned the need for instructions understandable by the non-technical housewife. Detergent compositions were discussed, particularly the so-called optical bleaches—the colourless blue-fluorescing substances used to give the "whiter-than-white" look. The danger of transfer of these substances from one article to another in the wash was pointed out and, in particular, the most objectionable effect upon the tint of textiles originally dyed to pastel shades such as peach and nil which, after contamination by the fluorescent optical bleach, appear pink and dirty blue.

Complaints of faults caused by the chemical bleach in the detergent powder, such as 10 per cent sodium perborate, were described; in particular of a royal blue dye on wool which develops yellow patches and spots at temperatures as low as 110° F. Cellulosic materials develop pin-holes either through the action of particles of the bleach which have not been completely dissolved, or through local traces of metal catalysts causing violent action by the dissolved persalt. Fading of dyes in sunshine while drying on the line may be attributed to incomplete rinsing of alkali. Some optical bleaches are themselves not fast to light and discolour in sunlight. The quite common practice of the housewife adding bleach containing chlorine to a detergent when washing whites leads to further troubles; Mr. Ward said that he understood that organic chloro-compounds are already being added to domestic washing powders in the United States and are being considered for use in Great Britain. He viewed this with the greatest concern, since it would lead to increase of complaints of loss of colour, fading, local bleaching, and loss of wear.

Mr. Ward concluded by saying that the housewife is puzzled by the number of products and the various claims made for them; whereas he had no objection to optical bleaches for those who want them for whites, he did complain that colours of textiles are spoilt by them, and argued that there should be available a detergent containing no bleach and no optical brightener.

Mr. F. P. Thompson (Unilever Ltd.) then spoke on the problem from the point of view of the manufacturer of detergents. He gave the typical compositions of washing powders of the soap (classical carboxylate) and non-soap (synthetic detergents) types, shown in Table 1. Both contain 0–1 per cent of sodium carboxymethyl cellulose and 0·02–0·08 per cent of optical bleach.

Table 1

Soap	(per cent)	Non-soap	(per cent)
Soap	40–65	Sodium alkylanyl sulphonates	20–22
Sodium carbonate	5–20	Other wetting or frothing agents	0–5
Sodium silicate	3–5	Sodium polyphosphates	30–40
Sodium phosphate	0–10	Sodium perborate	10
Sodium perborate	0–10	Sodium silicate	5
		Sodium sulphate	20

Mr. Thompson claimed that perborates have negligible effects upon most dyes and that oxygenated bleaches do not cause loss of strength of textiles. Perborates give better removal of some soils than manual scrubbing. With reference to the bright blue dye which turns green or yellow, he said that no change in shade is produced by carboxylate soap; with perborate it changes shade gradually, the effect being greater in soaps than in synthetic detergents. The change in colour increases with temperature and with concentration of suds. Loss of strength of textiles is least for the carboxylate soap; but with perborate it is much the same for all types of soaps and detergents.

Mr. Thompson spoke of many reports that no discoloration is caused by repeated washing with optical bleaches. He spoke of the difference between the skills and desires of the housewife and the technical expert, and also of the education of domestic users which is carried on by the makers of detergents.

Mr. G. S. J. White (Imperial Chemical Industries Ltd.) gave a brief account of the outstanding advances in the discovery of new dyes, pointing out that major new discoveries occurred at intervals of about thirty years. The requirements of a dye were listed as, first, ease of application; secondly, colour fastness and, to-day, fastness to detergents; and thirdly, colour gamut. Most attention has been given and most success achieved in making products easier to apply. On the other hand, those dyes most easily applied are least fast, and fastness requires more expensive dyeing processes. A striking demonstration was shown of a blue dye which, when made soluble by sulphonation, is applied easily but shows serious loss of colour on washing. When the dye is chemically bonded by the more expensive process of attachment by the cyanuric chloride reaction, only slight loss of colour occurs. When made soluble by a quaternary nitrogen atom and fixed upon the fabric by dequaternizing, it is fast to detergent; but this is the most difficult and expensive method of dyeing.

Mr. White recalled the pre-war German label guaranteeing fastness of dyed textiles to detergents and light, and mentioned the present 'Felisol' label controlled by an international committee which tests dyes and dyeings. He regarded the flow of information from the dye maker to the dye user as very good, but pointed out the paucity of the return of information and complaints from users. He estimated the annual world expenditure on research by dye makers as £15 million, of which about £4 million was spent on the salaries of chemists. He concluded by claiming that the problem of the ultimate consumer who still encounters textile goods of poor washing fastness can broadly find alleviation, if not entire resolution, within the textile industry itself, using the whole wide range of products of the dye manufacturers.

Dr. A. S. C. Lawrence (Sheffield), opening the discussion, said that it was clear that the main reason for the meeting was the composition of detergent mixtures; that the meeting was held to discuss whether the additional obligation laid upon dyestuff makers and textile manufacturers by the composition of detergent mixtures is, first, more than they can be reasonably expected to meet to protect the interests of their users and their own good name; and, secondly, whether this additional obligation is necessary for improving detergents or if it is a passing and unnecessary phase which will die out in a few years.

There were three stages in the development of detergents: first, their appearance on the market and the addition of builders to improve their action upon cotton; they were a boon, especially in hard water. The second step was that of adding a bleach, and the third was the addition of a white substance with blue fluorescence—the optical bleach to give the "whiter-than-white" look. This is a dye and a very bad one because it is not fast to detergents; it is now broadcast throughout the washtub. It might be possible for the dyestuff makers to produce an optical bleach that is fast. Alternatively, following Mr. Ward's suggestion of different products for different duties, Dr. Lawrence suggested three types of detergent; one, consisting of detergent and builder only for use in washing up, for paint, etc., and for all coloured and dark textiles; the second would contain also the bleach for occasional use on whites; and the third would have detergent, bleach and the fluorescent optical bleach for those who wanted it. The makers should sell each in a distinctively coloured package—say, red, blue or white—upon which their name and instructions should be printed. Members of the public have been so confused by advertisement campaigns that they either fail to read the maker's directions or mistakenly suppose that all brands are equally good.

Dr. Lawrence said that all the intelligent young women whom he had questioned said that they used only carboxylate soap for their clothes and synthetic detergents (often those containing the bleaches) only for domestic housework—a duty for which their formulation makes them unsuitable and uneconomical.

The basic reason for holding the meeting was the policy of marketing detergents which are compounded as Jacks-of-all-trades and masters of none. There seems to be a need for fundamental research into the nature of the soil responsible for the greying of whites and of the forces responsible for its persistent adhesion. The paradox which this material presents is that it is removed by the non-detergent components and not by the soap.

In the discussion, much evidence was given of complaints of faults arising during washing being reported to the manufacturer of the textile article. Patchy changes of shade due to the optical bleaches occur on twin-sets; rhodamine pink is not fast to detergents. The maximum degree of brightness from the optical bleach can be built up in an article free of it by washing in suds, containing none, from other articles which have been loaded. Faults due to the perborate chemical bleach include yellowing, said to be due to incomplete rinsing, and loss of colour, both generally and in spots. The latter were attributed to incomplete solution of the perborate in the hot water before the articles to be washed were put in. Two speakers said that they had seen advertisements for detergents on television in which this incorrect and dangerous procedure was shown. It was generally agreed that loss of strength is not a problem and that when it does occur, faulty rinsing is the cause. Bleaching on the line, especially during drying in sunlight, was also attributed to this cause. Serious disquiet was expressed at a report of the addition of bleaches containing chlorine to domestic detergents in the United States, and of their possible use in Britain.

A number of speakers made it clear that they considered that some detergent compositions, likely to cause damage to some textile goods of high quality, are being sold to housewives without adequate and sufficiently clear instructions. It is claimed by the manufacturers of these detergents that their inquiry and education services find none of the faults described. On the other hand, a manufacturer of baby clothes who guarantees to replace faulty goods has reported numerous complaints of change of colour, and said that a recommendation to use a selected detergent free from the objectionable additions has led to a large decrease in the number of complaints. He suggested clear classification of all detergents into two groups, one for whites and one for coloured goods. This and similar labelling proposals were received with applause by the meeting. It was stated that the dyestuff makers were unable to produce an optical bleach fast to detergents.

Dr. A. S. C. Lawrence, summing up, said that three main points had emerged from the meeting. First, that the light-fast dyes, which the dye maker can produce, require dyeing processes to make them fast to detergent compositions as now generally sold and this involves extra cost. Secondly, that the textile manufacturer receives the complaints, for the obvious reason that a woman who has purchased a relatively expensive article will complain to the shop where she bought it rather than write to the manufacturer from whom she has obtained a few pennyworth of detergent. Thirdly, that communication of highly technical matters to and from a technologically ignorant public is impossible, and the claims of success of inquiry and education services of the detergent manufacturers must be regarded with suspicion. New textile goods heavily loaded with optical bleach are already being sold, so that a ban on fluorescent brighteners in detergents would not be enough. It seems that some co-operative standard of labelling by makers of detergents, to distinguish in a simple and unequivocal manner for the ordinary housewife the basic types of composition, is the only satisfactory solution and one much overdue. Alternatively, makers of textiles will have to label their goods, specifying a safe detergent, until the makers of the present potentially harmful compositions, so widely sold, are driven to a more critical consideration of their duty to the public. A. S. C. LAWRENCE

FORESTRY IN THE UNITED KINGDOM

WHILE the Society of Foresters of Great Britain, having been formed in 1925, is the youngest of the British societies concerned with forestry, its membership is the most representative of the profession as, although it has an ordinary membership open to all who are interested, it caters primarily for the university graduate and others with equivalent qualifications. Its journal, *Forestry*, is published twice yearly. During the past year, it has published about a dozen original articles ranging over a very wide field, tending to be ecological rather than technical, though some of them link the two aspects; for example, a study of the effect of rate of growth on the density of timber.

The opening article in the 1958 volume is a thoughtful study by G. B. Ryle (at the time, the Forestry Commission director for Wales) on the social problems and possible developments in upland grazing areas where forestry is the obvious alternative use to sheep farming. A strong case is made for integration of farming and forestry, both uses being taken equally into account; action should be co-ordinated by combined councils and the mistakes of the past should be avoided. There have been faults on both sides, the agriculturist seeing the problem as one of maintaining the farm with the help of subsidies, etc., even when it is uneconomical, or less economical than alternative uses, while the forester has tended to overlook the fact that both winter and summer feed must be available to a sheep farm. Ryle also adduces fairly conclusive evidence that forestry gives more on-the-spot employment than sheep farming—probably twice as much—and stresses the need for improved housing as extensions of existing communities rather than new isolated centres.

A study of the mineral content of standing pine crops on the Culbin Sands by T. W. Wright and G. M. Will shows that a maturing crop with about 50 tons of dry organic substance contains about 170 lb. nitrate, 20 lb. phosphate, 100 lb. potassium, 160 lb. calcium and 32 lb. magnesium, of which about one-third to one-quarter is in the leaves and so returned to the ground annually; the wood, which alone is ultimately removed (provided the bark is peeled on the spot), contains less than one-fifth of the total. These figures, despite their smallness, are of considerable significance in relation to the very low mineral content of the blown sand.

Two papers deal with different aspects of a field that is attracting increasing attention, namely, the relation between the physical conditions, both natural and due to manipulation, under which trees are grown, and the properties of the timber they produce. Studies of site factors influencing growth are discussed in another two papers dealing, respectively, with wind effects and the measurement of light intensity. Taxonomic studies are represented by a paper on the elms of south Cambridgeshire and one on the named variants of the Scots pine. In view of the importance of the latter tree in afforestation and its wide distribution and range of forms, this analysis of 144 terms already published is a most useful contribution: it describes no less than twenty-six geographical varieties and twenty-five habit forms, together with many named variations in bark, foliage, cones, timber and seed.

The Royal Scottish Forestry Society was founded as the Royal Scottish Arboricultural Society in 1855 and its published transactions have developed into the current quarterly *Scottish Forestry*. While this Society draws its membership from a wider field than the Society of Foresters of Great Britain, and has a much bigger proportion of the non-professional element, its journal regularly includes original articles of considerable interest and value. Among those appearing during the year, mention may be made of a paper on the practical issue of using a knowledge of the life-history of the fungus (*Keithia*) which is liable to affect seriously the growth of *Thuja* seedlings, to raise healthy nursery stock of this tree; isolated nurseries used once only or in rotation, with due precautions to avoid sources of infection, are the solution. There is an interesting paper on the variation of susceptibility of European larch of different seed origins to frost, and another on 'group strike' by lightning, a case being reported of one hundred trees dying with only two showing actual scars, and a comparable case in a nursery. The morphological field is represented by a paper on bark variation in birch and its relation to figured wood.

The present Royal Forestry Society of England and Wales was founded in 1882 as the English Arboricultural Society, on similar lines to its Scottish counterpart. Its transactions appeared from 1884, becoming the *Quarterly Journal of Forestry* in 1907. As might be expected, a very similar range of original papers is being published, including in 1958 three on the properties of coniferous timbers as affected by treatment during growth, one on the effect of liming ploughed or unploughed upland moors, and one on the 'mechanized forest'.

Mention should not be omitted of the *Empire Forestry Review*, published quarterly by the Empire Forestry Association, which includes a proportion of original articles on British forestry among its much wider coverage; these are chosen primarily for their general interest though, of course, forestry issues are very similar all over the world. The chief items of this type in 1958 are on desirable road density in plantations and intensive methods of raising coniferous seedlings. In addition, there are the 'Men of the Trees' publishing *Trees* two or three times a year.

H. G. CHAMPION

FOOD INVESTIGATIONS

THE recently published report of the Food Investigation Board* for 1957 also covers the work of the Torry Research Station and the Humber Laboratory concerning the improved handling and processing of fish; the Low Temperature Research Station on meat, eggs and various plant foods; and the Ditton Laboratory and the Covent Garden laboratory concerned mainly with conditions of storage for fruit and vegetables.

A report of this nature provides an excellent illustration of the complexity of the problems associated with the maintenance of an all-the-year-round supply of food in an industrialized, urbanized community. In the main, the work is concerned with preserving food and this requires a study of differences in the initial state of the food, of the conditions of handling to which it may be subjected, and of methods of detecting early stages of deterioration, quite as much as a study of all aspects of the different methods of preservation, which include such varied means as the use of antibiotic ice, electronic radiation, electrostatic smoking, vacuum freeze-drying, gas storage, etc.

The Board stresses "the vital importance of the closest possible co-operation with the appropriate user industry from the outset of a research through all its stages to its final implementation". Several of the investigations concerning fish were made at the request of the White Fish Authority, the Herring Industry Board, and the National Federation of Fishmongers, and a committee of the National Farmers' Union was consulted when the research programme of the Ditton Laboratory was being planned. This is welcome collaboration and should not only ensure direction of effort towards the problems most urgently in need of solution but also speedy application of any solutions which might be found.

M. W. GRANT

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* Department of Scientific and Industrial Research. Food Investigation 1957: The Report of the Food Investigation Board with the Reports of the Superintendents of the Torry Research Station, the Low Temperature Research Station, and the Ditton Laboratory. Pp. vi+81. (London: H.M. Stationery Office, 1958.) 5s. net.

REMANENT MAGNETISM OF THE ALLARD LAKE ILMENITES

By CHARLES M. CARMICHAEL

Department of Geophysics, University College, University of Western Ontario

THE Allard Lake region of Quebec contains numerous outcrops of massive ilmenite enclosed in Grenville-type anorthosite of pre-Cambrian age. Hammond[1] has described the region, particularly the Lac Tio deposit, which is the largest of its type in the world.

Although the ore is usually referred to as ilmenite, it should be called hemoilmenite, since it consists of about 70 per cent ilmenite ($FeTiO_3$) and 25 per cent hematite (Fe_2O_3), with the remainder being largely composed of feldspar, pyroxene and pyrite. The massive ore consists of relatively large crystals averaging about 3–5 mm. in diameter. The hemoilmenite solidified originally in homogeneous crystals, and then upon cooling separated by exsolution into an ilmenite-rich phase and a hematite-rich phase. The hematite-rich phase has exsolved in the form of thin discontinuous lamellæ with their long and intermediate axes in the basal plane of the rhombohedral host-crystal. Thus the lamellæ have the general

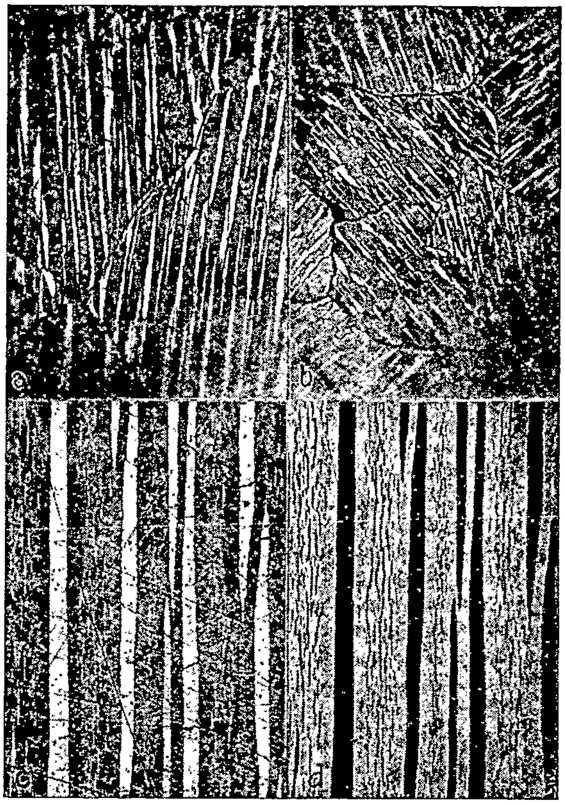

Fig. 1. Polished surfaces of hemoilmenite showing exsolved hematite lamellæ. The direction of the remanent magnetization is from top to bottom in each photograph

shape of thin elliptical disks with one long, one intermediate and one short axis (see Fig. 1).

The hematite lamellæ have exsolved in two distinct size-ranges (see Fig. 1*c*). The simplest explanation for this is that there are two plateaux in the cooling curve of the deposits : a long period of fairly constant temperature during which the large lamellæ exsolved, followed by a relatively rapid drop in temperature, and then a second constant-temperature period during which the small lamellæ were formed. The absence of small lamellæ in the ilmenite adjacent to the large lamellæ indicates a low hematite content, probably due to diffusion of ferric ions from the host into the large lamellæ. There are also small lamellæ of ilmenite in the central part of the large hematite lamellæ. Unfortunately, the steep sides of the hematite–ilmenite solvus curve as given by Nicholls[2] and modified by Uyeda (private communication in 1957 and ref. 3) make it difficult to fix the temperature plateaux accurately. However, the composition of the hematite-rich phase of 0·86 Fe_2O_3, 0·14 $FeTiO_3$ and of the ilmenite-rich phase of 0·87 $FeTiO_3$, 0·13 Fe_2O_3, as given by Uyeda (private communication, 1957) for one sample of Allard Lake ore, indicates a temperature during exsolution of about 700° C. or less. Thus it is not known whether the lamellæ were exsolved before or after they passed through their Curie point, which is about 580° C.

The directions of the remanent magnetization of samples taken from the deposits show a wide scatter, both in the angle of declination and in the magnitude of the angle of inclination, but the signs of the angles of inclination are all negative, that is, the north end of the magnetic vector is inclined above the horizontal. This accounts for the pronounced negative anomalies, in the aeromagnetic survey of the region, over the ilmenite deposits, as reported by Hammond[1] and Bourret[4]. Balsley and Buddington[5] have also reported negative aeromagnetic anomalies over hemoilmenite-bearing rocks in the Adirondacks.

There is a high correlation between the direction of the remanent magnetization of a specimen of the ore and the average direction of the long axes of the hematite lamellæ in the crystals which make up the specimen. In Fig. 1 the remanent vector lies in the polished surface and is directed from top to bottom in each photograph. This correlation between the direction of the remanent magnetization and that of the lamellæ has also been confirmed in single crystals large enough to be measured separately. This suggests that the present remanent magnetization of the ore is due mainly to the hematite lamellæ. Because of the shape effect, the lamellæ should retain only the component of their magnetization parallel to the long axis of each lamella, regardless of the direction of the magnetizing field. This is supported by the difference in intensity of the remanent magnetization of specimens similar in all respects except in the degree of alignment of the directions of the lamellæ from crystal to crystal throughout the specimen. The intensities of the remanent magnetization of the specimens photographed in Fig. 1*a* and 1*b* are, respectively, 0·028 E.M.U./gm. and 0·011 E.M.U./gm. Single crystals have been measured with intensities of more than 0·03 E.M.U./gm. and some massive samples have intensities of less than 0·005 E.M.U./gm.

A further test of the hypothesis that the remanent magnetic field is due to the hematite lamellæ was conducted by dissolving the hematite lamellæ out of the host ilmenite and comparing the intensity of the remanent magnetization before and after solution. Fig. 1*c* shows a typical polished surface and Fig. 1*d* the same surface after the exposed lamellæ of hematite had been dissolved out. Because the lamellæ are discontinuous and completely enclosed in the ilmenite phase, only those exposed on the surface can be dissolved. Thus thin sections of ore were used, ranging in thickness from about 2 mm. to 0·2 mm. Some typical results are shown in Table 1. There was no change in the direction of the remanent magnetization during the solution process. The sections used were cut so that the remanent vector lay in the plane of the section and so that the intermediate axes of the lamellæ were perpendicular to this plane in order to expose a maximum number of lamellæ at the surfaces. The sections with thicknesses of 2 mm. and 0·4 mm. were cut from specimens of typically massive ore of relatively high intensity, whereas the section 0·2 mm. thick was cut from a large single crystal about 12 mm. in diameter.

Since the present remanent magnetization of the ilmenite deposits is due to the exsolved hematite lamellæ and is directed in the average direction of the long axes of these lamellæ, the direction of the remanent magnetization is not necessarily the same

Table 1

Thickness of section (mm.)	Original intensity of magnetization (E.M.U./gm.)	Intensity of magnetization after surface lamellæ dissolved (E.M.U./gm.)	Decrease in intensity of remanent magnetization (per cent)
2·0	0·0264	0·0254	4
0·4	0·0281	0·0033	88
0·2	0·0322	< 0·0002	> 99·6

as that of the Earth's magnetic field which existed while the deposits were being magnetized. If the directions of the crystal axes throughout the deposits were completely random, it should be possible to determine the direction of the Earth's field at the time of cooling of the deposits by averaging the directions of the remanent magnetizations of a large number of samples. Unfortunately, the specimens from the Allard Lake deposits show marked alignment of the c, or principal, crystallographic axes of the grains, perhaps due to stress or other geological factors, so that little information about the Earth's field in the past can be obtained by measuring the direction of the present remanent magnetization.

Whereas only the Allard Lake ilmenites have been used in this investigation, it is probable that these results are applicable to other ilmenite deposits or rocks containing ilmenite of similar compositions, perhaps indicating that these rocks should not be used for palæomagnetic work. Investigations are continuing on other aspects of the magnetic properties of the Allard Lake deposits, including the reversed orientation.

[1] Hammond, P., *Econ. Geol.*, 47, 634 (1952).

[2] Nicholls, G. D., *Advances in Physics*, 4, 191 (1955).

[3] Uyeda, S., *Jap. J. Geophys.*, 2, No. 1, 1 (1958).

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[5] Balsley, J. R., and Buddington, A. F., *Econ. Geol.*, 53, 777 (1958).

ABSORPTION SPECTRA AND ASSOCIATED PHOTOCONDUCTIVITY OF PURE AND DECOMPOSED CRYSTALS OF THALLOUS AZIDE

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THE physical and optical properties of thallous azide (TlN_3) suggest that the lattice is predominantly ionic but some sharing of valence electrons occurs. This may be attributed[1] to the large difference in energy between the ionization potential of the thallium atom and the electron affinity of the azide radical. It has been found that thallous azide is a photoconductor when irradiated with light of wave-length corresponding to the fundamental absorption edge.

In the experiments to be described, the crystal of thallous azide was held against two platinum or silver electrodes in such a manner that the incident beam of light irradiated the major morphological face. Measurements were made with the crystal under vacuum and the photocurrent measured as a function of the wave-length of incident light. In addition, measurements have been made to determine the variation of photocurrent with intensity of the light.

The optical absorption spectrum of a single crystal of thallous azide is shown in Fig. 1. In addition to the long-wave-length tail, the absorption spectrum possesses a 'shoulder' in the vicinity of 3000 A. At shorter wave-lengths the absorption rises rapidly to the limit of measurement at 2000 A.

The spectral distribution of photocurrent in a pure crystal of thallous azide is shown in Fig. 2, curve *A*, where the applied voltage gradient was 60 V./cm. There is a subsidiary maximum in the photocurrent at 4300–4350 A. At wave-lengths less than 4000 A. the photocurrent increases rapidly. Measurements could not be made at wave-lengths less than 2600 A. as the output of light from the source used (xenon lamp) is very small at these wave-lengths. If silver electrodes are used instead of platinum electrodes, then the spectral distribution of photocurrent is similar to that of curve *A*, except that the rise in photocurrent at short wave-lengths does not occur until 3600 A.

The crystal used to obtain curve *A*, Fig. 2, was then irradiated, while still under vacuum, through a glass filter, by the output of light from a 100-W. mercury-vapour lamp. The spectral distribution of photocurrent was then measured and is given by curve *B*, Fig. 2. The applied voltage gradient was 160 V./cm. It will be seen that the photocurrent has been reduced to one-tenth of its original value and the rise in photocurrent at short wave-lengths has been eliminated. The maximum photocurrent occurs at 4250 A. The photochemical decomposition resulting from irradiation by the mercury-vapour lamp results in the formation of a thin film of thallium on the surface of the crystal. This metallic film gives rise to a new absorption band. In Fig. 3 the difference in absorption coefficients between an irradiated and pure crystal of thallous azide are plotted. Curves *A*, *B* and *C* of Fig. 3 show how this band develops with increasing time of irradiation.

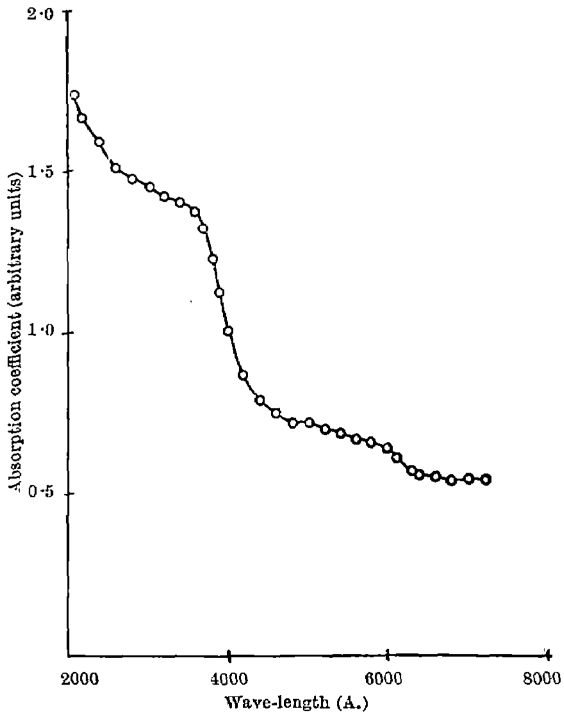

Fig. 1. The absorption spectrum of an undecomposed single crystal of thallous azide

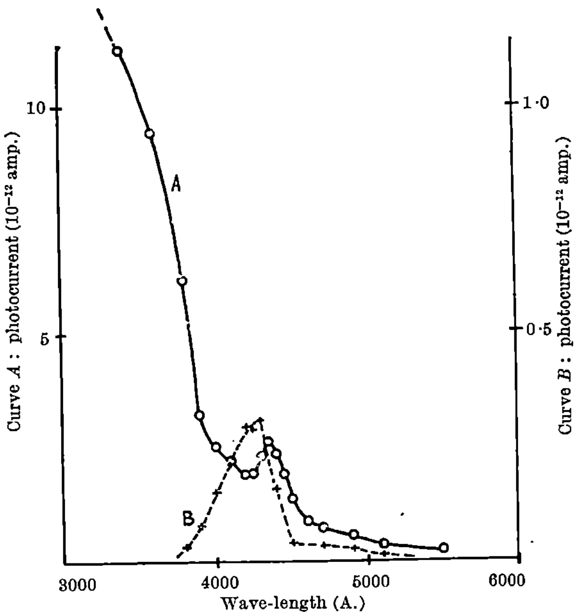

Fig. 2. Spectral distribution of the photocurrent in thallous azide at room temperature calculated for an equal intensity at each wave-length. Curve A undecomposed crystal; curve B photochemically decomposed crystal

The efficiency of photochemical decomposition increases with decreasing wave-length.

When a crystal of thallous azide (melting point 334° C.) is heated for 10 hr. at 230° C. metal specks are formed at the surface of the crystal. In this experiment, however, the metal is formed as relatively large discrete particles which can be up to 10^{-2} mm. in diameter. These particles appear in a matrix of apparently undecomposed thallous azide and do not give rise to a new absorption band as in the case of thallium produced photochemically. The spectral distribution of photocurrent of thallous azide decomposed thermally is shown in Fig. 4 (voltage gradient 80 V./cm.). There is a 'shoulder' at 4250 A., but the photocurrent rises sharply at shorter wave-lengths, as observed with pure thallous azide.

In order to obtain a uniform distribution of metallic thallium throughout a crystal of thallous azide, radioactive thallium-204 was used in the preparation of the thallous azide. These crystals were made by S. K. Deb. One year after preparation the crystals appeared black in reflected light and red in transmitted light. Metallic thallium is formed in the crystal by a mechanism similar to that described for silver azide[2] and also by irradiation damage due to the fast β-particles that are emitted during decay of the radioactive isotope. The intensity of the light source used in the previous experiments was not sufficient to give rise to a detectable photocurrent in these 'black' crystals. However, by using a 100-W. mercury-vapour lamp in conjunction with filters of narrow wave-band it was possible to show that the general features of the photocurrent – wave-length response resembled that shown in Fig. 4, although on a much reduced scale.

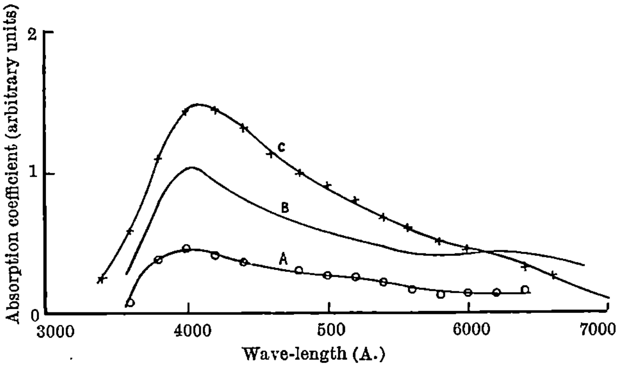

Fig. 3. Absorption spectra of thallium film formed during photochemical decomposition of thallous azide. Curve A, crystal irradiated for 1½ hr.; B, 4 hr.; C, 9 hr.

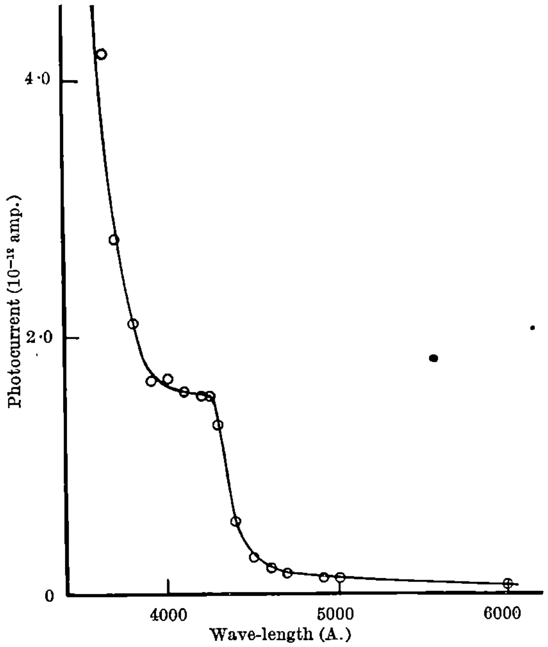

Fig. 4. Spectral distribution of the photocurrent in thermally decomposed thallous azide calculated for an equal intensity at each wave-length

In order to interpret these experimental results we first consider the photoconductivity of pure thallous azide given by curve A, Fig. 2. The subsidiary maximum at 4300–4350 A. may be identified with the thermal dissociation of optically formed excitons. The optical transition of electrons from the full band to the exciton band of the crystal gives rise to the 'shoulder' at about 3000 A. shown by the absorption spectrum of Fig. 1. The subsidiary photoconduction maxima are dependent on temperature and it was possible to determine an activation energy for the thermal dissociation of excitons in the thallous azide. The steep rise in photocurrent for wave-lengths less than 4000 A. arises from direct optical transitions from the full band to the conduction band of thallous azide. The corresponding optical absorption for this process is given in Fig. 1 by the steep rise in absorption coefficient at wave-lengths less than 3000 A. Hence over nearly the whole range of wave-length of curve A, Fig. 2, the observed photocurrent is the sum of two components. The first component, C_x, having a maximum at 4350 A., is the spectral distribution of photocurrent due to the dissociation of optically formed excitons by the thermal energy of the thallous azide lattice. The second component C_S is the spectral distribution of photocurrent due to direct optical transitions between the full band and conduction band of the crystal. Component C_S may be represented by an equation of the form[3]:

$$\frac{x}{\alpha} = \frac{1}{1 + \exp\{c(\varepsilon_0 - \varepsilon)\}} \qquad (1)$$

where c is a constant, ε is the energy of the incident light, ε_0 is the energy at the 'threshold' wave-length and x is the observed photocurrent which increases to a maximum value α (not measured). For $x \ll \alpha$ this equation may be written in the form:

$$\ln_e x = c\varepsilon + \ln_e \alpha - c\varepsilon_0 \qquad (2)$$

Curve A, Fig. 2, was plotted as $\ln_e x$ against ε and in this form (Fig. 5) yielded several points of additional information. It will be seen from Fig. 5 that for an incident light energy greater than 3·1 eV. the points of $\ln x$ lie on a straight line which changes to a line having a different slope for energies greater than 3·44 eV. This change in slope at $\varepsilon = 3\cdot 44$ eV. may be completely accounted for in terms of recombination, of conduction electrons and positive holes. When recombination occurs the electron – positive hole density is high (due to the increasing absorption coefficient) and the equilibrium photocurrent x^1, as measured, is given by $x^1 = x^{1/2}$, where x is the photocurrent that would be measured in the absence of recombination. Hence $\ln x = 2 \ln x^1$, and if this modification is applied it is found that the points of $\ln x$ for $\varepsilon > 3\cdot 44$ lie on a straight line having the same slope as that of $\ln x$ against ε for $3\cdot 1 < \varepsilon < 3\cdot 44$. This leads to the conclusion that $C_x = 0$ for $\varepsilon > 3\cdot 1$ and the spectral distribution of C_s can thus be determined for all ε. Knowing the contribution to the observed photocurrent of C_s it is thus possible to plot the spectral distribution of photocurrent due to C_x.

A similar analysis may be made for the photocurrent observed in thermally decomposed thallous azide. It is again found that recombination of electrons and positive holes occurs for C_s when $\varepsilon > 3\cdot 44$ eV. The spectral distribution of C_x so obtained is found to be identical in form (but reduced in amplitude) when compared with the spectral distribution of C_x for pure thallous azide, except that the maximum, as in Fig. 4, occurs at 4250 A., whereas for undecomposed thallous azide the maximum occurs at 4300–4350 A.

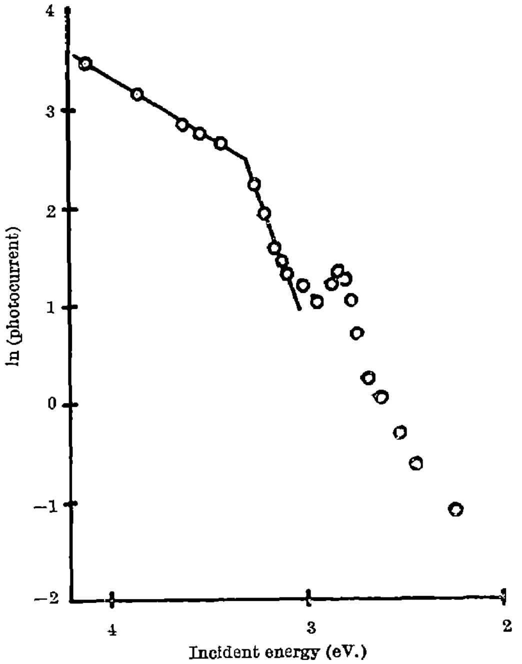

Fig. 5. Plot of ln (photocurrent) against energy of incident light, for curve A, Fig. 2

The spectral distribution of photocurrent obtained with photochemically decomposed thallous azide as given by curve B, Fig. 2, is identical to that calculated for C_x of thermally decomposed thallous azide with the important exception that curve B, Fig. 2, exhibits a long-wave-length tail between 4600 A. and 5200 A.

It has been found, as expected, that the long-wave-length side of C_x for pure and thermally decomposed thallous azide is of the form given by equation 2 and also that electron – positive hole recombination occurs in the vicinity of the maximum. It is therefore likely that the short wave-length decrease in photocurrent of C_x and shown, for example, by curve B, Fig. 2, is due to electron – positive hole recombination. The results so far described may be summarized, for example, with reference to the spectral distribution of photocurrent for undecomposed thallous azide given by curve A, Fig. 2. At long wave-lengths, namely, about 5000 A., the photocurrent due to $C_x + C_s$ is not inhibited by recombination. The absorption steadily increases with decreasing wave-length and the subsidiary maximum at 4300–4350 A. is achieved when recombination limits the rapidly increasing value of C_x. C_x then decreases to zero at 3980 A. (3·1 eV.). For wave-lengths less than 3980 A. the photocurrent is entirely due to C_s and this component is then unaffected by recombination until 3600 A. (3·44 eV.). In the absence of recombination, the photocurrent x will be proportional to I, the intensity of incident light. Where recombination limits the observed value of the photocurrent, then $x \propto I^{1/2}$. In order to verify these predictions involving recombination, the photocurrent of undecomposed thallous azide was measured as a function of the intensity of light at various wave-lengths. Table 1 gives the predicted and observed intensity – photocurrent relations

Table 1

Wave-length (A.)	Predicted	Observed
4650	I	I
4350	$I^{1/2}$	$I^{1/2}$
3800	I	c. I*
3350	$I^{1/2}$	c. $I^{1/2}$*

* Large error of measurement due to small intensity of light source.

The proposed mechanism of photoconduction in pure thallous azide is able to account quite well for the observed spectral distribution, but it still remains to explain the different photoconductive behaviour exhibited by pure and decomposed thallous azide.

In thallous azide decomposed thermally the metallic nuclei are present as discrete specks, the photocurrent has been reduced in magnitude and the minimum, which occurs at 4250 A. for pure thallous azide, has been lost because the maximum of C_x has moved to shorter wave-lengths and now occurs at 4250 A. If we assume that the metal specks, by attracting Tl^+ ions, act as electron traps, then if the number of such traps, N, is smaller than x^1, the number of conduction electrons, then $x^1 = x - N/2$, where x is the number of conduction electrons in the absence of such traps. The consequent reduction in density of conduction electrons will (a) reduce the observed photocurrent, and (b) move the maximum of C_x to shorter wave-lengths as the reduced electron density will delay the onset of recombination.

In the case of radioactive thallous azide the very large number of submicroscopic metal specks will lead to an overall reduction in photocurrent due to the increased absorption and the large number of traps. The spectral distribution of photocurrent should be as in Fig. 4, and this is what is observed.

Photochemically decomposed thallous azide, however, possesses a large number of metal traps in the form of a metal film on the surface of the crystal. This metal film also reduces the amount of light absorbed by the crystal in the region of C_x. The rise in photocurrent for short wave-lengths has been completely eliminated due to the metal electron traps. Similarly, as in the case of thermally decomposed thallous azide, the maximum of C_x has moved to shorter wave-lengths. However, the photocurrent has a long-wave-length tail and this arises from C_s. The metal film is not effective as an electron trap at these longer wave-lengths about 5000 A. because of the small absorption of the thallous azide. This means that the photoelectrons are produced some distance below the crystal surface.

In conclusion, it must be noted that if an 'undecomposed' crystal of thallous azide is irradiated on one of the minor morphological faces, then the spectral distribution of photocurrent is the same as that shown in curve *B*, Fig. 2. It has been found, however, that such crystal faces are far more sensitive to photochemical decomposition than the major faces, presumably due to their higher surface energy. Crystals examined in this manner have undoubtedly undergone some photochemical decomposition.

[1] Evans, B. L., and Yoffe, A. D., *Proc. Roy. Soc.*, A, **238**, 568 (1957).
[2] Deb, S. K., Evans, B. L., and Yoffe, A. D., *Nature*, **180**, 294 (1957).
[3] Moss, T. S., "Photoconductivity in the Elements" (Butterworth, London, 1952).

GENETIC CONTROL OF CHROMOSOME PAIRING IN INTERGENERIC HYBRIDS WITH WHEAT

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It has been shown that in hexaploid common wheat, *Triticum vulgare* ($6x = 42$), control of the purely bivalent-forming, diploid-like, meiotic behaviour is exercised by a gene, or genes, on one particular chromosome[1]. In the absence of this chromosome, pairing can take place between equivalent, homœologous, chromosomes in each of the three genomes, so that wheat ceases to behave as a classical autosyndetic allopolyploid. The diploidizing mechanism was exposed by Riley and Chapman in studies of 20-chromosome nullihaploids and 40-chromosome nullisomics in the variety Holdfast[1,2], and was indicated in the simultaneous work of Sears and Okamoto[3] on crosses of monosomics of the variety Chinese Spring with diploid wheat.

Chromosome V of Chinese Spring carries the gene responsible for the restriction of homœologous pairing but it has not yet been possible to confirm, by crossing, that the Holdfast chromosome, designated *HH*, with the equivalent effect is homologous with V of Chinese Spring. This is very likely, however, since both nullisomics have similar deviations from the euploid phenotypes, and it is known that the phenotype of nullisomic V is very different from those of all the other nullisomics of Chinese Spring[4]. Moreover, both chromosomes are similar in morphology, being heterobrachial with one arm about twice the length of the other.

The utilization of the variation of many diploid species in the genus *Aegilops*, and of *Secale* species, in the improvement of wheat is limited because there is little or no pairing between the chromosomes of wheat and those of the diploids with which wheat is combined in intergeneric hybrids, so that foreign genes cannot be introduced into wheat chromosomes by recombination. Riley and Chapman suggested that the genetic mechanism which restricts pairing between homœologous chromosomes of wheat might also be responsible for the failure of wheat chromosomes to pair with those of some species in related genera. If this were so, intergeneric hybrids deficient for the chromosome carrying the diploidizing control would have some chromosomes of wheat paired with some of those of the diploid parent. To test this hypothesis the crosses *T. vulgare* Chinese Spring monosomic V ($6x - 1 = 41$) × *Aegilops longissima* ($2x = 14$) and *T. vulgare* Chinese Spring monosomic V ($6x - 1 = 41$) × *Secale cereale* King II ($2x = 14$) were made. The monosomic parents in these crosses produced gametes with 20 or 21 chromosomes depending on whether or not the monosomic chromosome was included. Consequently, from the same female parent, hybrids with 27 or 28 chromosomes resulted from the combination of the seven chromosomes of the male gamete with the alternative female gametes. Hybrids with 28 chromosomes possessed, and those with 27 chromosomes did not possess, chromosome V of Chinese Spring which carries the pairing control gene.

Chromosome pairing at first metaphase of meiosis has been compared in 27- and 28-chromosome hybrids and data from a few of the plants examined are presented with those for euhaploid and *HH* nullihaploid plants (Table 1). The haploid data are those previously collected in the variety Holdfast since no comparable material was available in Chinese Spring. However, the meiotic behaviour of euhaploids in Chinese Spring is similar to that in Holdfast[3], and it is likely that nullihaploid V in Chinese Spring would have a meiosis similar to that of nullihaploid *HH* in Holdfast.

There was a mean of only 1·96 bivalents per cell in the 28-chromosome hybrid with *A. longissima* and there were never more than six bivalents per cell (Fig. 1). This is slightly higher pairing than in euhaploids, and since there is little homology within

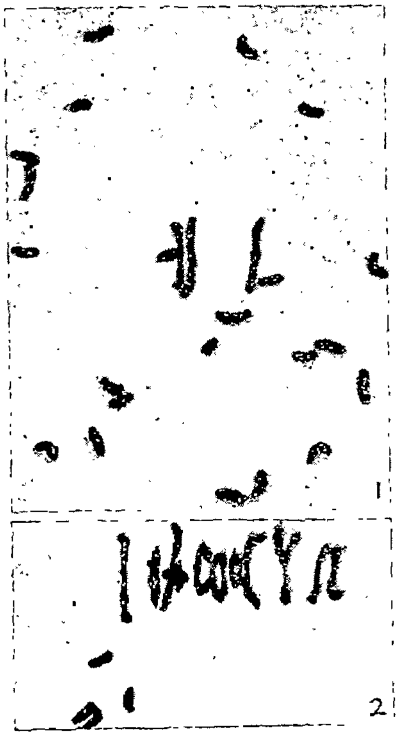
Table 1. MEIOTIC CHROMOSOME PAIRING IN HAPLOIDS AND HYBRIDS OF *T. vulgare* WITH AND WITHOUT THE CHROMOSOME CONDITIONING DIPLOID MEIOTIC BEHAVIOUR

Plant	Chromosome No.	Cells	Mean pairing				Range of chromosomes conjugated
			Univalents	Bivalents	Trivalents	Quadrivalents	
Euhaploid Holdfast	21	100	18·05 ± 0·20	1·38 ± 0·09	0·07	—	0–9
Nullihaploid Holdfast	20	75	9·02 ± 0·28	4·16 ± 0·12	0·86 ± 0·03	0·02	4–19
C. Spring × *A. longissima* 1	28	100	23·96 ± 0·23	1·96 ± 0·06	—	—	0–12
C. Spring × *A. longissima* 2	27	100	9·85 ± 0·33	6·45 ± 0·19	0·87 ± 0·09	0·41 ± 0·05	10–24
C. Spring × *A. longissima* 3	27	100	7·50 ± 0·35	7·58 ± 0·23	0·70 ± 0·08	0·56 ± 0·05	10–27
C. Spring × *S. cereale* 1	28	100	25·26 ± 0·21	1·37 ± 0·03	—	—	0–8
C. Spring × *S. cereale* 2	27	100	18·00 ± 0·26	3·18 ± 0·13	0·70 ± 0·09	0·11 ± 0·03*	4–17
C. Spring × *S. cereale* 3	27	100	17·83 ± 0·37	2·82 ± 0·14	0·89 ± 0·09	0·15 ± 0·05†	2–21

* Plus 2 associations of five.
† Plus 1 association of seven, 1 of eight and 1 of eleven.

the haploid complement of *A. longissima*[5] a small amount of pairing between wheat and *Aegilops* chromosomes must be indicated.

By contrast, chromosome pairing in the 27-chromosome hybrids with *A. longissima* was very high (Fig. 2). There were never fewer than 10 chromosomes paired and in some cells no chromosomes were left unpaired. The mean univalent frequency was almost the same as that of the 20-chromosome *HH* nullihaploid, so that the seven extra chromosomes were evidently often involved in pairing. Compared with the nullihaploid the mean bivalent frequency increased by more than half and the mean quadrivalent frequency increased 20 times, while there was about the same amount of trivalent formation. The frequent quadrivalents must have arisen from the conjugation of three homœologous chromosomes of some wheat groups with the equivalent *A. longissima* chromosomes. Apparently, therefore, the chromosomes of *A. longissima* will pair with those of wheat to a greatly increased extent when chromosome V is absent. For although quadrivalents are the only certain indication, presumably wheat and *Aegilops* chromosomes were also associated in bivalents and trivalents.



First metaphase of meiosis in Feulgen and orcein stained squashes of pollen mother cells of hybrids from the cross *T. vulgare* Chinese Spring monosomic V × *A. longissima*. (× 780)

Fig. 1. 28-chromosome hybrid with 3 bivalents and 22 univalents

Fig. 2. 27-chromosome hybrid with 1 quadrivalent, 1 trivalent, 8 bivalents and 4 univalents

The close relationship between *A. longissima* and *Aegilops speltoides*, the contributor of the *B* genome of *T. vulgare*, has been indicated by Riley, Unrau and Chapman[6]. Furthermore, the cytological affinity of all the genomes of wheat is shown by the intergenome pairing in *HH* nullihaploids, and from the pairing in hybrids between the putative diploid parents[1]. It is not surprising, therefore, that there is a close relationship between the chromosomes of *A. longissima* and those of each of the genomes of wheat. It is, however, remarkable that this affinity could normally be obscured by the diploidizing mechanism on chromosome V.

The amount of chromosome pairing in 28-chromosome hybrids between monosomic V and rye was not higher than that in euhaploid *T. vulgare* (Table 1). There is thus probably no pairing between wheat and rye chromosomes in normal hybrids. However, while there was much more pairing in the 27-chromosome hybrids from the same parents, and as many as 21 chromosomes could be involved in associations in one cell, there were on average fewer chromosomes paired than in *HH* nullihaploids of Holdfast. The 27-chromosome plants showed means of about one fewer bivalents per cell and this may reflect some interference, by rye, with pairing which occurs in nullihaploids. It is also possible, however, that the apparent differences may have resulted from the selection of cells scored, which was often compelled by the difficulty of interpreting cells with much pairing due to the attenuated and clumped nature of the chromosomes in rye hybrids deficient for chromosome V. The appearance of the chromosomes was normal in 28-chromosome hybrids with rye and in both types of *A. longissima* hybrid.

However, in the 27-chromosome hybrids there was about the same number of trivalents as in nullihaploids, but more than four times as many quadrivalents. The quadrivalents must have resulted from associations of homœologous chromosomes from each of the three genomes of wheat with a rye chromosome. Since rye chromosomes could pair with wheat chromosomes in quadrivalents it may be that they were also conjugated with wheat chromosomes in bivalents and trivalents. However, the frequency of rye–wheat pairing must have been low compared, for example, with the amount of *A. longissima*–wheat pairing. Nevertheless the evidence of quadrivalents alone is sufficient to show that, in the absence of V, rye and wheat chromosomes can pair, even though this rarely, if ever, happens in euploid hybrids.

Furthermore, in the 27-chromosome hybrids with rye, there were some large complexes, associated by chiasmata, and involving up to eleven chromosomes. These occurred in about five per cent of first metaphase cells but were often so complex that they defied interpretation and so such cells are under-represented in the analyses recorded. The large complexes probably arose because there is not a strict one-to-one relationship between rye chromosomes and wheat homœologous groups; rather, certain rye chromosomes must have affinities with the chromosomes of two wheat groups. That is, the rye chromosomes differ from chromosomes of the wheat groups by translocations, and for associations of more than eight to occur the rye complement must differ from the wheat genomes by at least two translocations involving three pairs. Annual rye differs from perennial rye by two translocations involving three chromosome pairs[7]. If the translocations which differentiate the rye species are the same as those which differentiate annual rye from the wheat genomes, then there would be no associations larger than quadrivalents in 27-chromosome hybrids involving perennial rye. If this could be shown it would indicate the primitive structure of the perennial rye genome and the derived nature of the annual rye genome, and so would clarify the general understanding of the origins and phylogeny of cultivated rye.

The chromosomes of rye and *A. longissima* show marked differences in their capacity to pair with wheat chromosomes in the absence of chromosome V. In view of the present evidence on the genetic control of pairing, the dangers of drawing phylogenetic conclusions from pairing in hybrids are apparent. Nevertheless, the differences between the rye and *Aegilops* derivatives may, with caution, be taken to indicate the greater evolutionary divergence of rye and wheat, compared with *Aegilops* and wheat, further evidence of which is the failure of rye chromosomes fully to match the wheat groups.

The present evidence on the powerful influence of the diploidizing control of hexaploid wheat on chromosome pairing in hybrids leads to two main conclusions. First, it is apparent that the possible influence of genetic situations such as that in wheat must be taken into consideration whenever chromosome pairing in hybrids involving polyploids is used in the interpretation of phylogenetic relationships. The chromosome pairing in crosses with polyploids should be compared with that in hybrids with the diploids from which the polyploids were derived. The effect of genes isolating the genomes of the polyploids and interfering with the expression of pairing affinities at meiosis might then be detected.

Secondly, since it is apparent that the barrier to the pairing and recombination of wheat chromosomes and those of some related species in other genera can be removed by the exclusion of chromosome V, the reservoirs of genetic variation upon which the wheat breeder can now draw are greatly increased. All the diploid species of wheat and *Aegilops* are comparatively closely related and have chromosomes capable of pairing in diploid hybrids[8], so that this complete group can be regarded as a single pool from which genes may be extracted and incorporated on wheat chromosomes by recombination. This process will be limited only by the capacity to make appropriate crosses and to devise means of handling the hybrid material. Numbers of manipulations of 27-chromosome material are possible. Hybrids may be back-crossed directly with wheat, or may be treated with colchicine to produce 54-chromosome, multivalent-forming amphiploids also to be used in back-crossing. These amphiploids may be infertile and hard to maintain, and it will then be necessary to use the amphiploid sectors on the original *F*1 plants treated with colchicine for back-crossing.

Similar techniques may be used to exploit the pairing which can be induced between rye chromosomes and wheat chromosomes. Consequently it may, at last, be possible to combine rye and wheat without resorting to breeding amphiploids or whole chromosome addition and substitution lines. The complications to be overcome in handling the derivatives of nulli-V hybrids should not be under-estimated. Nevertheless the exploitation of these hybrids holds unique possibilities for extending the genetic variation of wheat, although a full estimate of the potentialities must be deferred until genetical results are available.

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ABSCISSION-ACCELERATORS IN LUPINS (*LUPINUS LUTEUS* L.)

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In nearly all recent publications the initiation of abscission is considered to be primarily controlled by auxin[1–4]. Osborne[5,6], however, was the first to publish evidence that an abscission-accelerating factor other than auxin is produced in senescent leaves or with induced senescence of normal green leaves. This natural abscission factor was found to counteract the abscission-delaying effect of indolylacetic acid in bean explants and was claimed not to be a sugar, amino-acid, purine or pyrimidine.

Recently, it was found in our laboratory that a natural abscission-accelerator is produced not only in senescent organs, but also in the rapidly growing fruits of lupins (*Lupinus luteus* L. var. Weiko II), and that this abscission-accelerator has a very powerful inhibiting effect on the growth of wheat coleoptile sections as well.

Young pods were collected seven days after flowering, when they were quite small (mean weight 135 mgm.), but had just entered their period of rapid growth, and were most active in inducing abscission

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of further flowers[7]. The purification of ether extracts, chromatography and coleoptile straight-growth test were the same as reported recently[8]. The results of one chromatogram of the acid fraction of such an extract are illustrated in Fig. 1, and this shows the presence of one growth promotor (A) ($R_F = 0{\cdot}4$–$0{\cdot}5$), and of one powerful inhibitor (B) ($R_F = 0{\cdot}55$–$0{\cdot}75$; solvent isopropanol : 25 per cent ammonia : water = 8 : 1 : 1).

Although B caused up to 90 per cent inhibition of coleoptile extension (the residual growth occurred mainly during the 2-hr. soaking period of the cut sections), it did not appear to have a toxic effect, the sections did not change colour, remained fully turgid, and were capable of assuming growth at a rapid rate after rinsing them in distilled water and adding indolylacetic acid to the medium. Yet, the activity of B in lupin pods was 1,000 times greater than that of inhibitor β from an equal amount of etiolated pea seedlings extracted under identical conditions[8].

Interactions between various concentrations of B and indolylacetic acid were measured, and some of the results in Fig. 2 show that the effect of B can be counteracted by certain concentrations of indolylacetic acid, amounts of 1 and 3 μgm. indolylacetic acid per ml. being able to neutralize the inhibiting effect of B extracted from 230 and 700 mgm. of tissue, respectively.

A and B were extracted separately from their corresponding areas on the chromatograms, to test their activity in the lupin abscission test, which essentially was an adaptation of Addicott's bean abscission test[9]. The explants used in our test consisted of a 2-cm. section of the main flower stalk with the five pedicels half way, and the flowers removed. Directly after cutting, the explants were placed upright in 5-mm. thickness of 2 per cent agar, which was allowed to set in 9-cm. crystallizing dishes, covered by a Petri dish lid. The purified extracts were reduced in volume and applied to punched paper disks in a wide range of concentrations, or they were mixed with small quantities of lanolin paste, which were then applied to the explant, either to one of the proximal sides (the physiological base of the flower stalk, because substances were preferably translocated in apical direction), or to the distal side of the abscission zone (cut end of the pedicel).

Results in Table 1 show that with proximal application abscission is accelerated by both substances

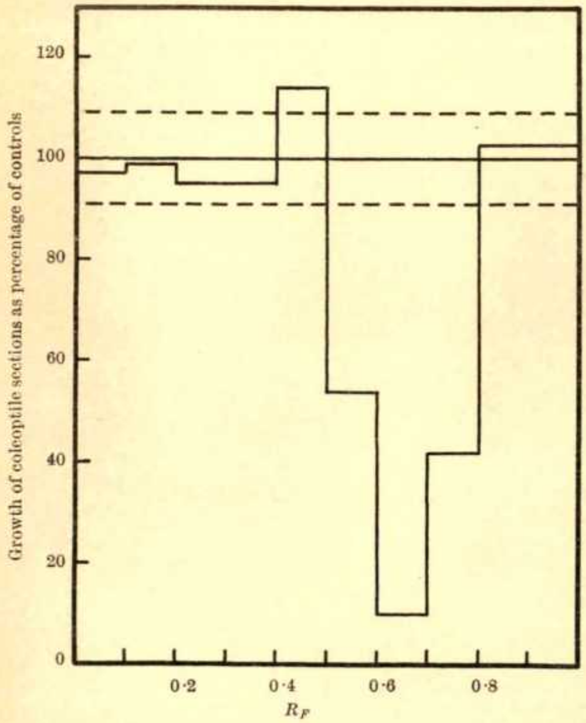

Fig. 1. The response of wheat coleoptile sections to chromatogram strips prepared from the acid fraction of an extract of 10 gm. of lupin pods. Solvent, isopropanol : ammonia 25 per cent : water (8 : 1 : 1). Growth plotted as a percentage of growth of control sections (8·41 mm. over a period of 17½ hr.). The broken line represents the level at which differences were significant ($P = 0{\cdot}05$)

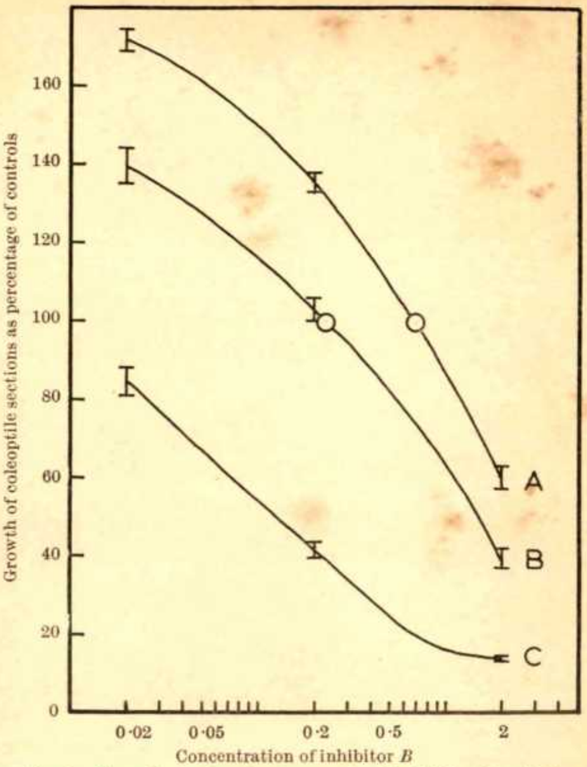

Fig. 2. The effects of various amounts of indolylacetic acid in alleviating the growth inhibition caused by various amounts of inhibitor B (all quantities per 1 ml. medium; vertical lines, 2 × standard error). Curve A, 3 μgm. of indolylacetic acid; B, 1 μgm. of indolylacetic acid; C, no indolylacetic acid added. Abscissa, the equivalent fresh weight of tissue (gm.) from which inhibitor B was extracted

Table 1. EFFECT OF TWO ENDOGENOUS GROWTH SUBSTANCES IN LUPINS ON THE NUMBER OF HOURS REQUIRED FOR 50 PER CENT AND COMPLETE ABSCISSION, RESPECTIVELY

	Hr. to 50 per cent abscission	Hr. to complete abscission
Proximal application		
Control	81·4	115
Inhibitor *B* equivalent to 5 gm. of tissue	64·5	84·5
Inhibitor *B* equivalent to 1 gm. of tissue	81·9	97·5
Promotor *A* equivalent to 5 gm. of tissue	74·9	93·5
Promotor *A* equivalent to 1 gm. of tissue	81·1	100
Distal application		
Control	87·2	134
Inhibitor *B* equivalent to 250 mgm. of tissue	72·0	89
Promotor *A* equivalent to 500 mgm. of tissue	130·5	—

A and *B*. With distal application, however, *B* accelerated abscission and *A* delayed it. Thus, *A* behaved like a true auxin as in Addicott's auxin-gradient theory[1], and *B* like the abscission-accelerating factor extracted by Osborne from senescent leaves.

It was concluded previously that the abscission-inducing effect of developing pods on subsequent flowers could not be explained in terms of auxin only[10]. At present, it appears likely that flowers on basal whorls, which are first to open, are capable of producing pods because, both substances being produced distally to the abscission zone, *A* will counteract the abscission-accelerating effect of *B*. However, once both substances have entered the flower stalk, they are preferentially translocated in the apical direction, and being proximal to the abscission zones, they both would be expected to co-operate in accelerating abscission of further flowers.

Further details of this work, and of comparisons made between virus-infected (low incidence of abscission) and healthy plants, and of changes occurring during the development of pods will be reported elsewhere.

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'CHLORIDE-SECRETORY' CELLS IN THE GILLS OF TELEOSTS

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CURRENT theories concerning the regulation of water and salts by teleost fishes involve the hypothesis that some ions, principally chloride, are transported against the concentration gradient into a freshwater fish and out of a marine fish. The ability of certain acidophil cells in the gills to bring about this ion movement has come to be generally accepted, although the original claim for this function of the acidophil cells[1] has been contested more than once. Keys and Willmer described the undeniable existence of large numbers of secretory cells in the gills of eels and other teleosts (Fig. 1: all sections were stained with hæmatoxylin-eosin and alcian blue). They estimated that there were between 3 and 6 million cells in an eel weighing 250 gm. and that they constituted "a probable and even possible histological basis for branchial chloride excretion" which had previously been demonstrated[2,3]. The elasmobranch *Scyliorhinus* was found to lack these cells in the gills, which accorded well with the interpretation of osmoregulation in these fish. Experimental evidence for a salt-regulating function for the cells was put forward by Liu[4], who found that their development was favoured by a gradually increasing salt concentration.

Observations on the estuarine mudfish *Fundulus* gave support to the 'Keys-Willmer' theory[5,6], and Getman[7] similarly found differences between secretory and absorptive phases of the cells in the eel. Copeland and Pettengill[8] together demonstrated that enzymic activity could be localized within the cells, thus providing a possible physiological mechanism for chloride exchange.

More recently, Vickers[9] has suggested that the cells represent a metaphasic form of mucous cells. The gradual acclimatization of fish to high external salinities induced the development of the cells. Histological changes were associated with the secretory phase. A large amount of circumstantial evidence has thus been accumulated in favour of a chloride-secretory function.

There has also been some criticism of the 'Keys-Willmer' theory. Krogh[10] was sceptical of a chloride-secretory function of the cells and the absence of any direct evidence justifies this. Bevelander[11] made a comparative study of many fish and suggested that the 'chloride-secretory' cell was a mucous cell. The work of Copeland and Pettengill on *Fundulus* to some extent discredited Bevelander's study; but it is interesting to recall it in the light of Vickers's more recent conclusions. Bevelander found the acidophil cells in the mucous membranes of the mouth and gill cavities, and their presence in the general buccal-branchial region was confirmed in *Fundulus*[12]. Investigations of the acidophil cells in teleosts have demonstrated that their greatest development is in the pseudobranch[13] (Figs. 1–3). The pseudobranch, whether it is represented by the simple gill-like structure in the herring, or the more complex enclosed mass in the salmon, consists of large acidophil cells held compactly by connective tissue, with a well-developed capillary blood supply. This picture is essentially the same in marine, freshwater or

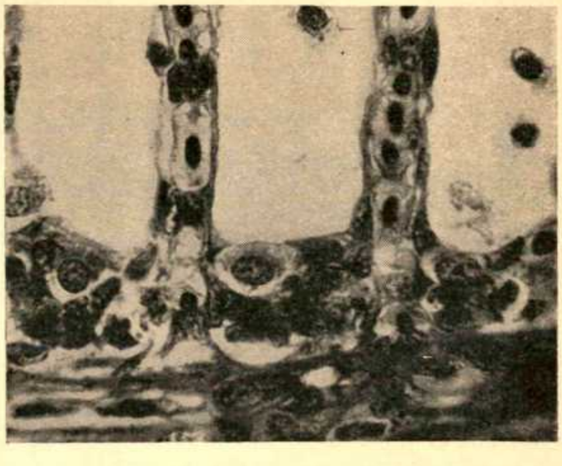

Fig. 1. Photomicrograph of T.S. gill lamellæ of salmon smolt in fresh water to show detail of acidophil cells. (× *c.* 700)

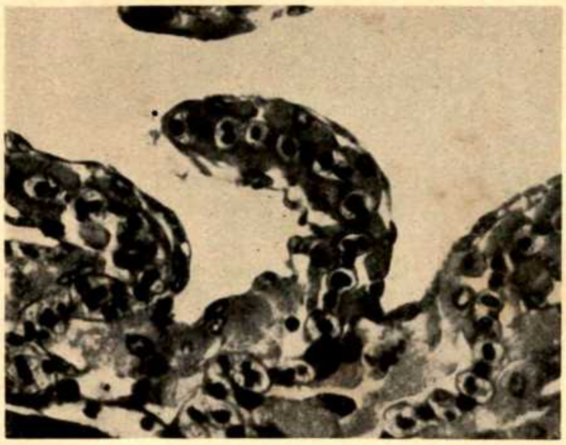

Fig. 2. Photomicrograph of T.S. pseudobranch of young herring in sea water. (× *c.* 600)

migratory species. The acidophils of both gills and pseudobranch are regarded as the same cells[13]; if their identity is established, then it is important to reconsider their function.

The presence of similar acidophil cells in both freshwater and marine teleosts presents another aspect of the problem. Some of the authors quoted have seen histological changes, and attributed them to changes in the polarity of the cells, when the fish are living in different environments. The presence of the cells in regions where they could not function as chloride regulators and their apparent absence in newly hatched fish larvæ, where regulation takes place, also create doubts as to the general validity of the theory. The anatomical disposition of the pseudobranch, for example, is such that the blood supply is from the first efferent gill artery; within the pseudobranch it becomes a capillary network; and after anastomosis it goes principally as an ophthalmic artery to the eye. Thus, the blood reaching the pseudobranch has already passed the respiratory and ion-regulating gills. It must be fully oxygenated, with no appreciable load of bicarbonate which could be broken down by the carbonic anhydrase present. The acidophil cells of the pseudobranch and other parts of the branchial region thus have a very different internal environment from those in the gills. In addition, while the pseudobranch hangs freely into the branchial cavity in a few teleosts, in many it has sunk below the epidermal surface.

Experiments designed to investigate the function of the pseudobranch in some teleost fishes are in progress and are being conducted along two lines:

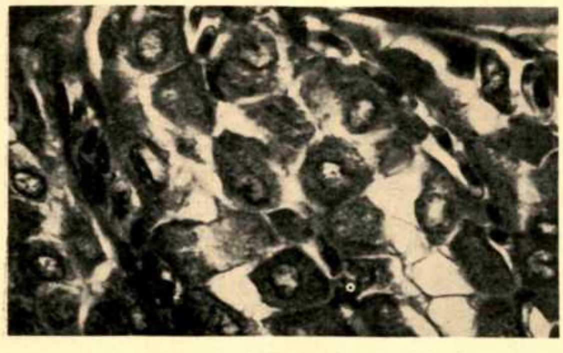

Fig. 3. Photomicrograph of T.S. pseudobranch of salmon smolt in fresh water. (× *c.* 600)

(1) The osmoregulatory ability of bilaterally pseudobranchectomized fish and normal fish in different salinities is being compared.

(2) The rate of ion transport in operated and normal fish is being compared, using radio-isotopes.

Preliminary results do not suggest that the pseudobranch is a major site of osmoregulation within the range of salinities 0–3·5 per cent. In a number of species (herring, saithe, sea trout, rainbow trout) the pseudobranch can be removed on both sides either by heat cautery or by a surgical technique. No significant difference in survival-times could be found between those sea water fish replaced in sea water or in isotonic medium ($\frac{1}{3}$ sea water), freshwater fish replaced in fresh water, and controls. All species of fish were seen to feed within a day or two of the operation; there were no external signs of distress. The majority of the fish are still alive some 2–3 months after the operation, and no increase in the acidophils of the gills of these fish has been observed (Fig. 4).

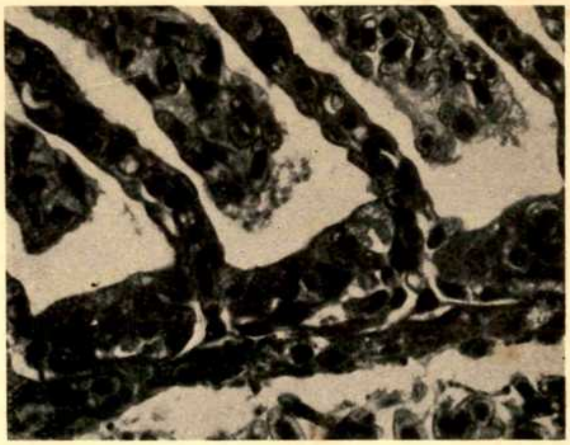

Fig. 4. Photomicrograph of T.S. gill lamellæ of adult sea trout in sea water three months after pseudobranchectomy. (× *c.* 600)

Since the fish appear to achieve osmoregulation in fresh water or sea water after pseudobranchectomy, should we conclude that the cells of the gills alone are able to cope with osmotic stresses of the magnitude?

If the cells of the pseudobranch do not function as chloride-regulators, we are justified, in the absence of any direct evidence, in asking if the very similar cells of the gills do act in this way. In short, are the acidophils of both gills and pseudobranch concerned with salt-exchange at all? It is hoped that a more complete investigation of the function of the pseudobranch will help to answer this question.

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

A High-resolution Survey of the Andromeda Nebula at 408 Mc./s.

In December 1958 observations of the Andromeda Nebula were made using the 250-ft. radio telescope at Jodrell Bank[1]. A Dicke type radiometer, pass-band 408 ± 2 Mc./s., noise figure 6 db., was used. The beam was elliptical, having half-power widths of 40 and 56 min. of arc. The system was calibrated using radio source 14*N*5*A*, which was assumed to have a flux[2] of 47×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$. Figs. 1, 2 and 3 show the intensity contours of the nebula, averaged scans along the major and minor axes, and an actual record of a scan through the nebula.

Previous lower-resolution surveys at 158 Mc./s. and 237 Mc./s. have shown[3,4] that the radio emission from the nebula can be divided into two components, one co-extensive with the visible nebula called the disk component, and accounting for 10 per cent of the total emission, and the other a much broader elliptical component, called the corona, extending over 10° along the major axis and 6° along the minor axis.

The outstanding new feature shown by this high-resolution survey is the complex structure of the corona, in particular the spur-like extensions away from the major axis (Fig. 1). Some structure is also seen in the radiation from the disk component. The greater part of the radio emission from the disk lies above the dotted line on the minor axis scan (Fig. 2) and appears to come from a source coincident with the optical centre. This peak is not broader than the beam, so that an upper limit of 35 min. of arc can be set for the diameter of this central source of radiation. At the points marked by arrows on the major-axis scan in Fig. 2, the profiles of optical and radio emission both show a change of slope. It is interesting to note that this is the brightest part of the spiral-arm structure of the nebula.

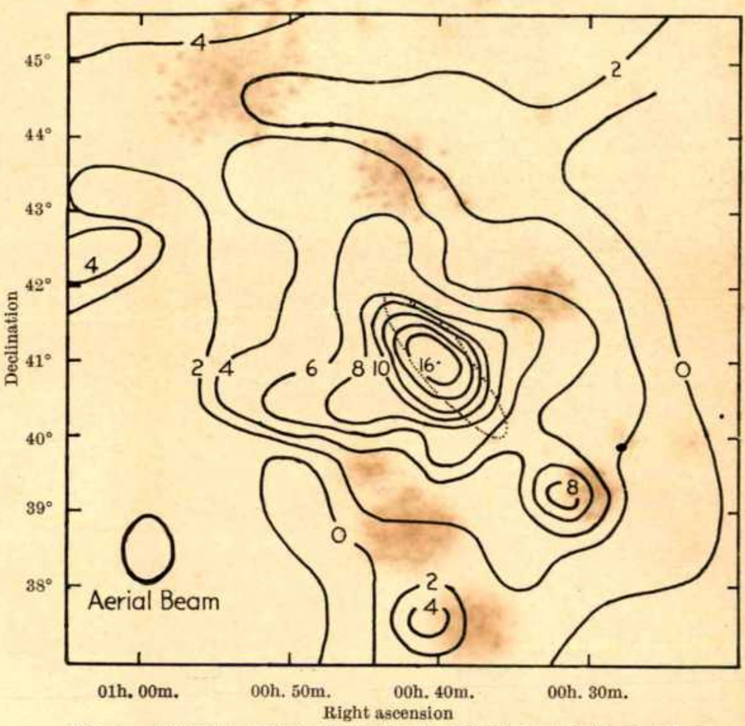

Fig. 1. 408 Mc./s. radio contours of the Andromeda Nebula plotted in intervals of 2 deg. K. brightness temperature, indicating the temperature above a chosen reference region, R.A. 00h. 15m., dec. + 38°. The dotted ellipse shows the 24·05 mag.²/sec.² contour taken from a recent photometric survey by de Vaucouleurs (ref. 8) of the nebula. The co-ordinates are for epoch 1950.0

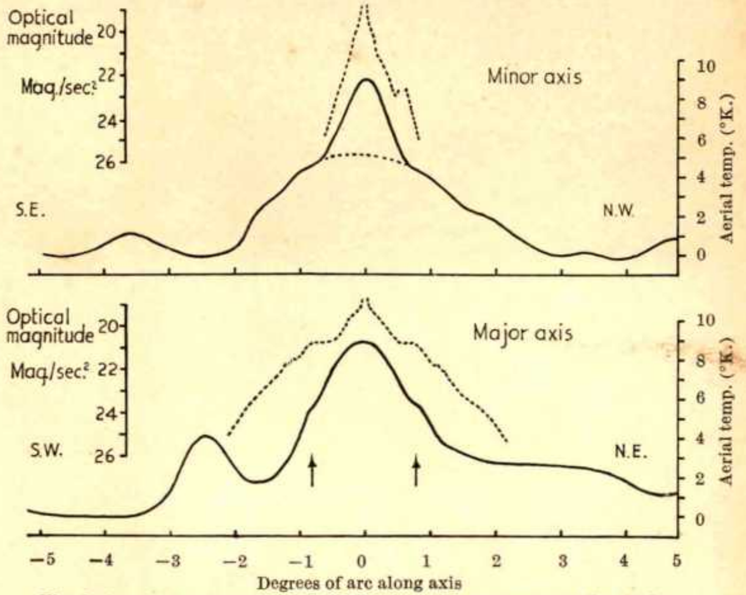

Fig. 2. Averaged radio scans along the major and minor axes of the Andromeda Nebula. In each case the major axis of the beam lay within a few degrees of the major axis of the nebula. The dotted curves are the corresponding photometric profiles obtained by de Vaucouleurs (ref. 8)

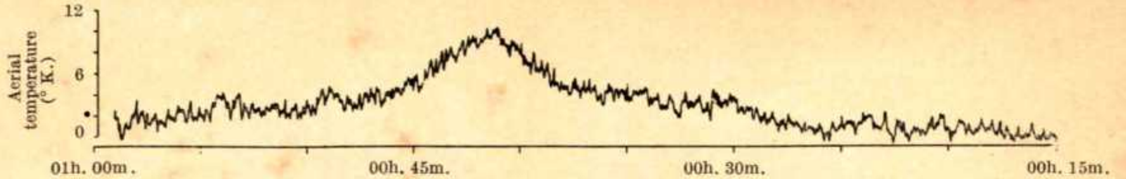

Fig. 3. A typical drift curve through the Andromeda Nebula at + 40° 15′ declination

Assuming that the corona extends to the 2° K. contour (Fig. 1) the total emissivity is 140×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$, of which the disk component contributes 8×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$. The general background temperature has been assumed to be 1 deg. K. above the reference temperature, and this has been subtracted before measuring the emissivity. The extended 'plateau' to the north of the nebula has been included, although it is not certain that it is associated with the nebula.

The radio sources (R.A. 00h. 31m. 45s., dec. + 39° 12′, flux $4 \cdot 5 \times 10^{-26}$ W.m.$^{-2}$ (c./s.)$^{-1}$; R.A. 00h. 34m. 30s., dec. + 38° 24′, flux $1 \cdot 5 \times 10^{-26}$ W.m.$^{-2}$ (c./s.)$^{-1}$) have been assumed not to lie in the nebula, and their emissions have been subtracted in deriving the figure for the total emissivity. The source (R.A. 00h. 40m. 30s., dec. + 37° 36′) lies outside the assumed limits of the corona. It has a flux of 3×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$.

The fainter satellite of Andromeda, N.G.C. 205 (R.A. 00h. 37m. 40s., dec. + 41° 25′), is an irregular elliptical galaxy (E_5, $m_p = 8 \cdot 9$)[5]. No radio emission has yet been detected from an elliptical galaxy or any similar structure (for example, a globular cluster) devoid of interstellar gas[6]. It is important to decide how much elliptical galaxies radiate relative to normal spiral galaxies, so that the importance of interstellar gas in the production of radio radiation may be assessed. An upper limit of 2×10^{-26} W.m.$^{-2}$ (c./s.)$^{-1}$ may be placed on the flux from N.G.C. 205 at 408 Mc./s., by examination of the contours in Fig. 1. This is less than 70 per cent of the radiation from a normal spiral galaxy having the same photographic magnitude. This calculation is based on a value given by Hanbury Brown and Hazard (private communication) for 158 Mc./s. radiation, that $m_r - m_p$ is equal to $0 \cdot 5$ for normal S_b galaxies, if m_r is defined as $m_r = - 53 \cdot 45 - 2 \cdot 5 \log S_{158}$. The spectral index is taken to be $- 1 \cdot 1$.

The nature of the spur-like extensions of the contours (Fig. 1) is at present a matter for speculation. In the left-hand spur, some indication of fine structure is seen in the original records. The records show two sources of a few flux units at positions R.A. 00h. 46m. 15s., dec. + 40° 24′ and R.A. 00h. 52m. 00s., dec. + 40° 30′. If these sources are subtracted, the spurs then appear symmetrical. Similar north and south polar spurs have been detected in the radio emission from our own Galaxy[7], and although they are not as prominent as the spurs in Andromeda, it is possible that such spurs are structural features common to spiral galaxies. In Andromeda, the angle made by the line of extension of the spurs to the minor axis is what would be expected if the synchrotron mechanism[9] were responsible for the emission. This suggests that the magnetic fields in the corona of the nebula may be ordered, and related to the spiral arm structure.

We thank Prof. A. C. B. Lovell for making available the facilities at Jodrell Bank, and Mr. R. Hanbury Brown and Dr. C. Hazard for suggestions and criticisms throughout the course of the work. One of us (D. S. M.) gratefully acknowledges a Leverhulme Research Fellowship.

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March 24.

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Fine Iron Filaments Magnets

It has been known for many years that a body containing parallel elongated and suitably equispaced iron particles, each of about $0 \cdot 02 \mu$ cross-sectional diameter, should theoretically possess excellent permanent magnetic properties. To the best of our knowledge, all attempts at producing materials with the desired structure have relied on the manufacture and compacting of submicroscopic iron particles. Although the results have been of considerable scientific and commercial interest, the desired degree of uniformity of particle characteristics has not yet been achieved.

In an endeavour to avoid some drawbacks of previous methods, we have developed a technique of drawing compacts containing parallel iron wires embedded in a copper alloy matrix until the iron wires become invisible filaments and the compacts acquire a high intrinsic coercive force. Values of 300–700 oersteds have been obtained so far. (Patent applications have been filed in Australia and overseas countries in respect of these methods and materials.)

Provided the materials within the compacts and the reducing methods are suitably selected, it is possible to preserve a fair uniformity of the iron cross-sections and spacings until the filaments are a few microns in diameter. Below the limit of optical microscopic resolution, magnetic measurements suggest that the iron filaments are excellently aligned and that some of them satisfy the theoretical requirements even when their estimated equivalent diameter is smaller than $0 \cdot 1 \mu$.

Fig. 1 shows the median intrinsic coercive forces of the individual filaments at infinite spacing, estimated from magnetic measurements of the best compacts produced so far. These results have been obtained only in very fine brittle wires drawn under conditions of extreme cold work and then annealed. More ductile compacts, allowing further reductions, have generally produced lower

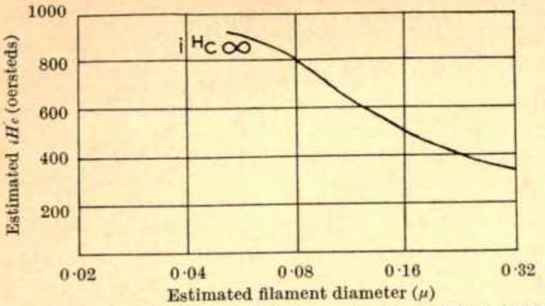

Fig. 1. Estimated median intrinsic coercive force of the individual filaments at infinite spacing versus estimated filament cross-sectional diameter

coercive forces at any given estimated equivalent filament diameter.

Members of the staff of the Division of Tribophysics of the Commonwealth Scientific and Industrial Research Organization have greatly contributed to the success of this preliminary investigation. Thanks are also due to the British Iron and Steel Research Association for supplying a sample of very pure iron wire.

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Sintering of Quartz Crystal

The transformation of quartz into cristobalite at temperatures higher than 1,470° C. has hitherto been accepted as a direct process. Recent measurements of the kinetics of this reaction (unpublished work) have, however, shown that the process is indirect and consists of two consecutive reactions in which a non-crystalline, disordered silica phase appears as an unstable intermediary between the quartz and the cristobalite.

During this work, quartz particles heated at 1,500–1,570° C. were observed to sinter in the early stages of the reaction so strongly as to convert the original loose powder to a hard mass and to reduce the rate of reaction substantially. This effect occurred before any cristobalite had developed and ceased once cristobalite became abundant, when the mass reverted to powder. The purity of the quartz used (Brazilian crystal) ruled out the possibility of any fluid phase except from the quartz itself. It therefore seemed likely that the intermediate non-crystalline phase was responsible for the sintering.

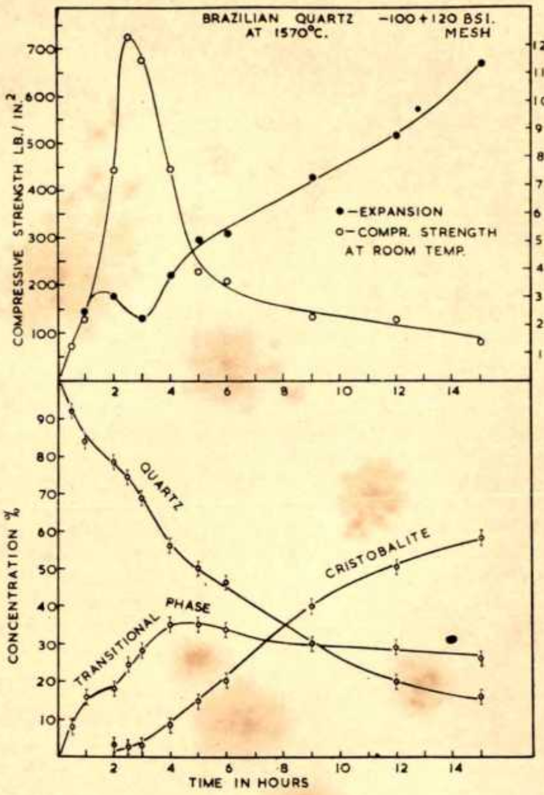

Fig. 1

These effects were studied further by measuring the compressive strength and the linear expansion or contraction, both at room temperature, of pressed cylindrical specimens after firing for various periods at 1,500°, 1,530° and 1,570° C. The results for Brazilian quartz crystal (average diameter 0·137 mm.) at 1,570° C. are shown in Fig. 1. The mineralogical constitution of each sample was determined by differential thermal analysis, which is now established as a reliable method for this purpose[1].

It will be seen that, in the early stages of the reaction, the quartz was transformed solely into the intermediate phase; at the same time, the compressive strength rose rapidly and shrinkage took place. Following the appearance of appreciable

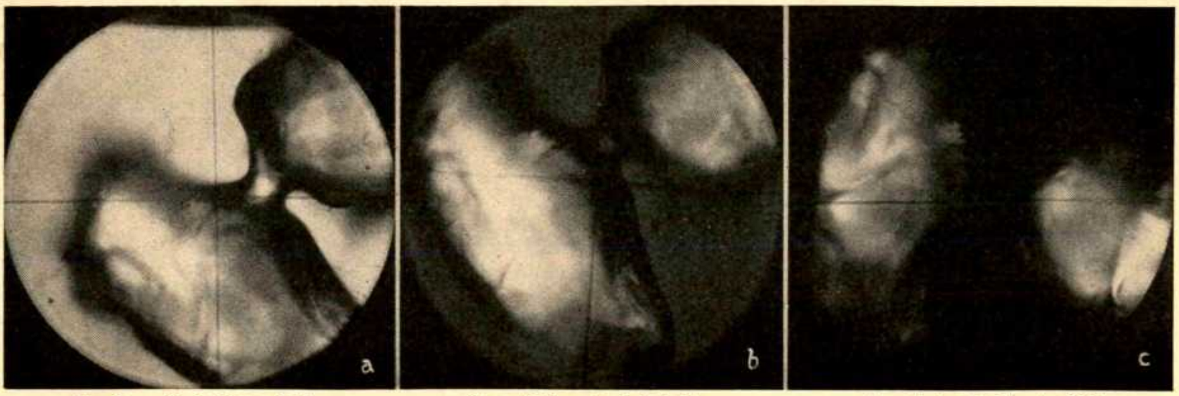

Fig. 2. (*a*) Ordinary light; (*b*) partially polarized light; (*c*) polarized light. (× 200)

amounts of cristobalite (namely, after 3–4 hr.), the strength diminished rapidly; expansion again occurred as the result of the continued conversion of quartz into forms of lower density.

Sintering and shrinkage of pure oxides at high temperatures are usually attributed to diffusion and the formation of 'necks' or lenses at points of contact between the particles. Examination of the quartz under the microscope showed that this mechanism was operative. Fig. 2 illustrates typical examples of the abundant neck-growth found after firing for 2½ hr., when about 20 per cent of the intermediate phase and virtually no cristobalite had developed. Fig. 2*a* is in ordinary light; Figs. 2*b* and 2*c*, in polarized light with partial and total extinction respectively, clearly indicate the intermediate phase as a continuous isotropic layer surrounding the residue of the quartz crystal and forming the neck between the particles. Sintering in quartz thus appears to take place via the disordered surface layer developed at high temperatures and is not inherent in the crystal. The rapid drop in strength on continued heating suggests that cristobalite is similarly deficient in sintering characteristics at the temperatures used. Full details of this work will be published shortly.

This work is part of a programme made possible by the award of an 1851 Senior Studentship to one of us (A. C. D. C.), and we thank the Royal Commission for its support.

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CHEMISTRY

Ionization Potentials of Electron Donors

Recently, Briegleb and Czekalla[1] have described a method of determining the ionization potentials (I_p) of electron donors from the frequencies (ν) of the charge-transfer bands of the complexes of these donors with certain electron acceptors. This is based on a non-linear theoretical relationship between I_p and ν.

Similar results may be obtained from an empirical linear relationship between I_p and ν; this is sufficient to correlate the experimental values of I_p and ν. Such relationships have been determined for complexes of donors of reliably known ionization potential[2] (namely, benzene, toluene, *m*-xylene, mesitylene, naphthalene, 1-methylnaphthalene and aniline) with the electron acceptors chloranil (C), *p*-benzoquinone (Q) and 1,3,5-trinitrobenzene (T) respectively. These are:

$$I_p = 5{\cdot}13 + 1{\cdot}39 \times 10^{-4}\ \nu_C$$
$$I_p = 4{\cdot}61 + 1{\cdot}33 \times 10^{-4}\ \nu_Q$$
$$I_p = 4{\cdot}25 + 1{\cdot}39 \times 10^{-4}\ \nu_T$$

for solutions in carbon tetrachloride, where I_p is in electron volts, ν in cm.$^{-1}$, and the subscripts to ν indicate the appropriate electron acceptor.

From measurements of frequencies of charge-transfer bands of complexes of these three acceptors with other donors in carbon tetrachloride, the ionization potentials may be evaluated. Examples are quoted in Table 1.

Table 1

Donor	Ionization potential (eV.)				
	Calc. from ν_C	Calc. from ν_Q	Calc. from ν_T	Mean	Ref. 1
Durene	8·0	8·2	8·3	8·2	8·4
Pentamethylbenzene	7·9	7·9	7·9	7·9	—
Hexamethylbenzene	7·8	7·8	7·8	7·8	7·9
Anthracene	7·4	7·4	7·4	7·4	7·4
N,N-Dimethylaniline	7·3	7·3	7·1	7·2	—
N,N,N',N'-Tetramethyl-*p*-*p*'-diaminodiphenylmethane	7·1	7·0	7·1	7·1	—
N,N,N',N'-Tetramethyl-*p*-phenylenediamine	6·7	6·7	6·7	6·7	—

For aromatic electron donor molecules, save those of very low ionization potential where it is improbable that such relationships are justified, this method may provide a simple means of estimating ionization potentials which may be difficult to determine by other methods, such as Rydberg series, photo-ionization and electron impact, because of practical details such as the low vapour pressure of some of these substances.

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Radioassay of Aqueous Solutions mixed with Solid Crystalline Fluors

I have previously described a new approach to direct radioassay of aqueous solutions of weak beta-ray emitting isotopes in the liquid scintillation spectrometer[1]. The aqueous solution was intimately mixed with a mass of finely divided beads of clear plastic into which a fluor (diphenylstilbene) has been incorporated (Pilot *B*-Beads, Pilot Chemicals, Inc., Watertown, Mass.). We wish to report that a number of crystalline fluors, more efficient, less expensive and more generally available, can be substituted for the plastic and used in an analogous fashion despite their poorer light-transmitting qualities[2]. For example, in a slurry made up of 0·7 ml. $Na_2{}^{14}CO_3$ and 0·5 gm. diphenyloxazole the carbon-14 was counted with 27 per cent efficiency. Instead of trying to hold the solid fluor in stable suspension, which can be done with the help of thickeners such as glycerol, it has proved more satisfactory to let the fluor settle to the bottom of the vial. Addition of a detergent is essential to ensure prompt and uniform wetting of the crystals. The performance of a fluor depends not only on its inherent fluorescence efficiency but also on the size and shape of the crystals, since the closeness of packing determines the mean free path of beta-particles through the solution before they encounter a fluor crystal. Best results thus far have been obtained using blue-violet fluorescence-grade anthracene crystals (Distillation Products Industries, Rochester, N.Y.). This highly purified material was three times as efficient as ordinary 'chemically pure' anthracene. The difference may in part reflect the presence of trace impurities in the latter, known to shift the fluorescence to higher wave-lengths. Even different lots of fluorescence-grade anthracene may differ by 20–30 per cent in efficiency, but the material in any given lot gave excellent reproducibility without further treatment. A routine technique currently used in our laboratories for carbon-14 and tritium is described.

Exactly 1 gm. of anthracene is weighed into a ·5-dram counting bottle (T. C. Wheaton Co., Millville, N.J.), 3 ml. of the unknown solution (containing 1 : 1,000 'Triton *GR*-5', Rhom and Haas Co., Philadelphia, Pa.) is pipetted on to the mass of anthracene and the mixture is stirred, breaking up any clumps of crystals. After an hour to allow the crystals to settle completely, the vial is ready for counting. The count-rate does not appear to be sensitive to temperature in the range 0–25° C., but freezing can alter the count-rate, depending on the extent to which radioactive solute becomes concentrated adjacent to the crystals during freezing. Counting in the present study was done in the Packard liquid scintillation spectrometer with a box temperature of approximately 2° C., photomultiplier voltage 1,345 V. (tap 10) and 'window' setting 10–∞. Under these conditions absolute efficiency for carbon-14 in 3 ml. of solution is 20 per cent; for tritium, 0·5 per cent. Background-rate is 90–110 c.p.m. At 1,200 V. background is only 65 c.p.m. and efficiency is only 10 per cent less than it is at 1,345 V.

As shown in Fig. 1 smaller volumes added to the 1 gm. of anthracene are counted with considerably higher efficiency (maximum of 54 per cent for carbon-14, 2·3 per cent for tritium when only the crystals at the top are wetted) but reproducibility is less satisfactory and quenching correction with internal standard cannot be easily made. Above 3 ml. sample volume, further addition of a sample of the same specific radioactivity in c.p.m./ml. does not further increase the observed count-rate. Reproducibility of the routine method is shown by replicate analyses of an aqueous solution of alanine-1-^{14}C, which gave standard deviations of 3·6 per cent (7 samples) and 4·1 per cent (5 samples). Three sets of four replicate samples of tritiated water were counted with a maximum range of ± 3·5 per cent. Quenching due to materials with absorption spectra overlapping the emission spectrum of anthracene is corrected for by adding an internal standard of the appropriate isotope in a volume of 0·05 ml., stirring and recounting. The validity of such a quenching correction is shown by the results in Fig. 2.

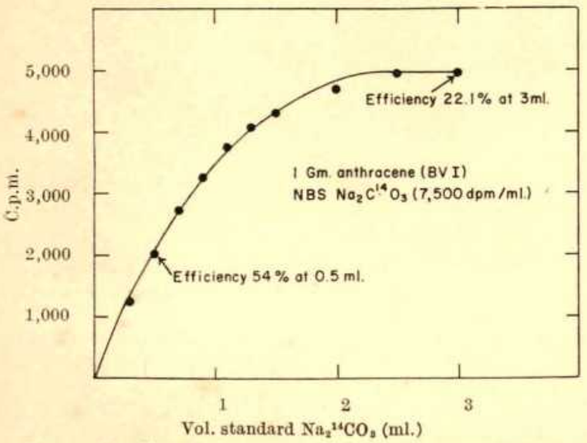

Fig. 1. Counting efficiency as a function of volume of solution added to a fixed amount of anthracene

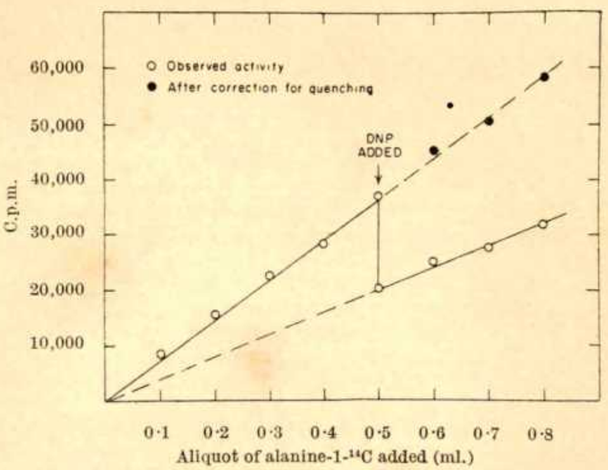

Fig. 2. Correction for quenching. The indicated aliquots of alanine-1-^{14}C were added to a vial containing 1 gm. of anthracene and 12 ml. of water containing 1 : 1,000 'Triton'. 2,4-Dinitrophenol was added at the point indicated

The method has been successfully applied to solutions of proteins, glucose, amino-acids and sodium carbonate in water or in buffer and to proteins and sodium carbonate in sodium hydroxide. It should be applicable to any material soluble in aqueous solvents and not reacting with anthracene. It has been shown that small molecules such as sodium carbonate, glucose and amino-acids can be quantitatively recovered by washing the anthracene. This feature of the method may be particularly valuable when only small amounts of sample are available and a radioassay is desired prior to further studies. Another important application of the method is in the counting of material of low specific activity when large amounts are available. If the material does not quench the fluorescence, it may be concentrated to high levels so that many milligrams are counted at the indicated efficiency. Larger amounts of anthracene have also been used (for example, 12 ml. of solution with 6 gm. anthracene) and even though the efficiency does not go up linearly (a large fraction of the emitted light comes from the upper surface of the anthracene mass) this permits considerably higher absolute count-rates. It may make feasible the counting of polar compounds with specific radioactivity too low to count in the conventional liquid scintillation systems, considering the limitations in sizes of sample sometimes involved.

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Derivatographic Investigation of the Anthracite of the Don

The anthracite of the Don has been investigated by the derivatographic method of F. Paulik, J. Paulik and L. Erdey[1]. By this method it is possible, by a single, automatically recorded measuring process, to obtain not only the thermogravimetric curve showing the change in weight of the sample (*TG* in Fig. 1) but also the rate of loss of weight (*DTG*) and

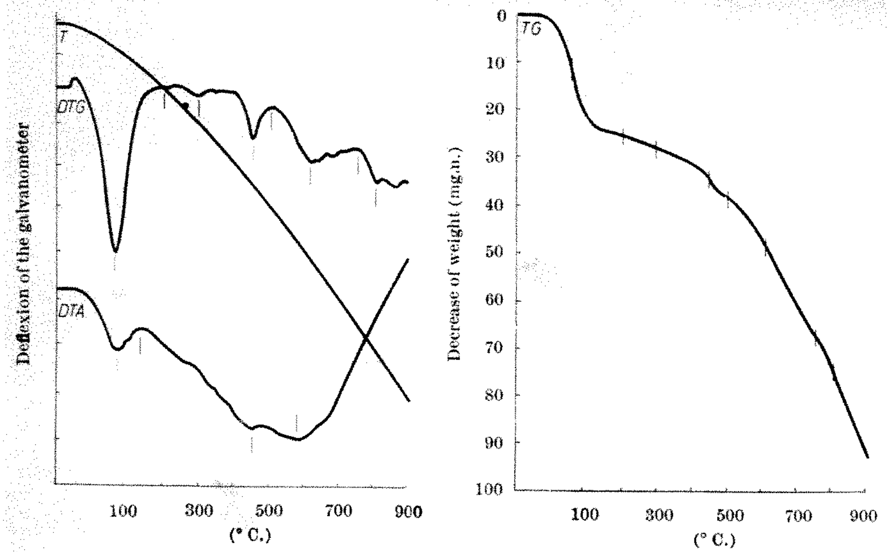

Fig. 1

the differential thermal analysis curve (*DTA*), giving information on the changes in temperature during thermal decomposition. The temperature curve (*T*), with the assistance of a calibration curve previously photographed on the paper, gives the temperature corresponding to each point obtained.

The immediate analysis of Don anthracite is as follows: ash, 9·4 per cent; combustibles, 90·6 per cent; coke, 96·3 per cent; carbon fix, 86·9 per cent; volatiles, 3·7 per cent.

By adjusting the sensibility of the balance, its full-scale deflexion was made to correspond to a change of weight of 100 mgm. A rate of heating of 5 deg. C./min. was maintained from room temperature to 900° C. Experiments were carried out in a stream of nitrogen (15 l./hr.).

The maximum rate of release of water vapour from the sample (water content, 2·5 per cent) occurs at 80° C. An endothermic maximum on the *DTA* curve occurring at 85° C. corresponds to this peak in the release of water. As only a relatively small part of the water is driven off in the temperature-range above 100° C., it appears that water is bound mainly by absorptive forces in the anthracite, chemical forces playing a relatively insignificant part.

A small peak occurs on the *DTG* curve at 295° C. This peak is of great interest, as it shows that atomic groups and structures characteristic of cellulose and plant residues are still conserved—though to a small degree—in anthracite.

In the derivative thermogravimetric study of peats and peat constituents[2], a high peak was reported at 300° C. in the thermal decomposition of cotton cellulose. When projecting the data of the *DTG* curve on the *TG* curve, it can be seen that this characteristic cellulose structure is present in only 0·3 weight per cent in anthracite, presumably in the form of side-chains.

The decomposition peak at 350° C., characteristic of humic acids, does not appear at all on the *DTG* curve of the anthracite.

The next peak of the *DTG* curve occurs at 450° C. This maximum is analogous to the main peak in the decomposition of bituminous coals, the position of which was found to vary between 390° C. and 420° C., according to the quality of the bituminous coal. As the temperature of decomposition is a function of the rank of coal, and the peak of decomposition is shifted towards higher temperatures with higher ranks of coal, it is not unexpected that in the case of anthracite—the last of the series—it should occur at 450° C.

It was found in an earlier investigation, by comparing the results of derivatographic analysis with those of dilatometric tests, that the main peak on the decomposition curve corresponds to the resolidification temperature T_3, that is, to the beginning of coke formation. Although anthracite does not pass into the plastic state through the action of heat, and consequently no resolidification takes place, it can reasonably be supposed, on the analogy of bituminous coals, that the peak exhibited by anthracite at 450° C. also marks the initial temperature of coke formation.

These observations are in good agreement with the X-ray results reported by Lermusiaux and Quinot[3]. They conclude from the radiograph of anthracite that the structure of anthracite contains particles of 5·7 A. radius, consisting of 84 carbon atoms, which are distributed in two layers, spaced at 3·4 A. from one another. The individual particles are linked together by oxygen-bridges.

The evolution of gases, consisting chiefly of carbon monoxide and carbon dioxide, in the temperature range 200–500° C. can be attributed to the rupture of these oxygen bridges. Above 500° C. a substantial change occurs in the radiograph. A structure of 12 carbon atoms characteristic of coke appears. The particles consist of two graphite hexagons, 3·4 A. apart; whereas in coke from bituminous coals the particles are strongly linked by carbon atoms and radicals formed of cracked bitumen, the hexagons in coke from anthracite are not linked together materially.

My derivatographic investigations suggest that coke formation begins at 450° C. This result agrees well with the X-ray results mentioned above, as it is obvious that coke formation must have progressed to a certain degree before the coke structure becomes observable radiographically. Above 500° C. the character of the evolved gases also changes, and the gases released consist chiefly of hydrogen. The appearance of hydrogen may be ascribed to the depolymerization of the 84 carbon-atom structure and the formation of the 12-carbon graphite hexagons:

$$C_{84} \rightarrow 7\,C_{12}$$

The *DTG* and *TG* curves suggest that the structure characteristic of bituminous coals contributes only 0·7 per cent to that of the anthracite, but as it is split off in a relatively limited temperature interval of not more than 100 deg. C., it is easily observable.

The most important quantitative changes in anthracite occur above 500° C. The loss of weight in the range 500–800° C. amounts to 3·5 per cent. The changes in this region, which exhibits a further peak above 600° C., appear to be due to strong depolarization of the anthracite structure.

It should be mentioned that the values for volatiles obtained derivatographically are somewhat higher than those from immediate analysis, probably because of the slower rate of heating.

The *DTA* curves show that the peak at 450° C. analogous to the decomposition peak of bituminous coals, and the decomposition peak above 500° C. characteristic of depolymerization are both endothermic.

Derivatographic results with anthracites from another source may possibly be somewhat different from those obtained for the Don anthracite ; nevertheless, since the structure of different coals becomes more similar with higher rank, great differences are not to be expected in the thermal decomposition of individual anthracites.

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MINERALOGY

Variation in Etch Behaviour of Jacobsite with Different Cell Dimensions

During the study of polished sections of manganese ores from the Kodur Group of mines, Srikakulam Dt., Andhra Pradesh, India, I came across three different types of jacobsite, associated with other manganese minerals like braunite, hausmannite, pyrolusite, cryptomelane, coronadite and γ-MnO_2. It is the interesting variation in the colour and etch behaviour in the different types of jacobsite that attracted my attention, and investigations to find out the cause of such variation were attempted.

Of the three different types of jacobsite, one occurs as a homogeneous mineral, pseudomorphous after garnet, whereas the other two types are in widmanstatten intergrowth with hausmannite. Of the last two types, one exhibits all the characters of normal jacobsite as described by Ramdohr[1] and Uytenbogaardt[2]. It is non-pleochroic olive-grey in colour with reflecting power of 19·6 per cent in green light in air, isotropic and negative to all standard reagents. It is the second type of jacobsite in intergrowth with hausmannite that exhibits altogether different colour under reflected light, and its reactions to etch reagents are also different. It is rose-brown in colour with reflecting power of 20·01 per cent in green light in air. It reacts with concentrated hydrochloric acid in 1½ min. and the solution turns greenish-yellow. With hydrofluoric acid, the mineral is instantaneously etched black with corroded surface ; the etching is much faster than in the hausmannite exsolution lamellæ. All these characters are very similar to those exhibited by magnetite, though the mineral was conclusively identified as jacobsite by X-ray powder analysis (Table 1). All the different types of jacobsite yielded similar *d* spacings, though their other characters vary considerably.

To investigate the possible cause of this peculiar etch behaviour of jacobsite, the cell dimension of all the three types was measured and the results are given in Table 2.

Table 1. Measured *d* Spacings and Intensities of Jacobsite. Iron/Manganese Radiation

d (A.)	*I*	*d* (A.)	*I*	*d* (A.)	*I*
4·86	4	2·42	1	1·72	2
2·975	4	2·105	4	1·619	5
2·542	10	2·024	2	1·489	7

Table 2. Cell Dimensions of Jacobsites

Description	Cell dimension
1. Homogeneous jacobsite pseudomorphous after garnet	$a = 8·506$ A.
2. Jacobsite, olive-grey in colour, unetched by any standard reagent, in intergrowth with hausmannite	$a = 8·483$ A.
3. Jacobsite, rose-brown in colour, etched by hydrochloric acid and hydrofluoric acid, in intergrowth with hausmannite	$a = 8·410$ A.

According to Mason[3], the cell dimension of jacobsite increases with increased amounts of manganese in structure. In Table 2, the first type of jacobsite has the largest cell dimension ($a = 8·506$ A.), which, according to Mason's[3] diagram (p. 146), contains a fair amount of manganese in excess of minimum. This excess manganese could not exsolve, apparently due to lack of proper temperature. The second type of jacobsite has all the characters of true jacobsite, and its cell dimension compares favourably with any normal jacobsite in the vredenburgite field. The third type has a much smaller cell dimension ($a = 8·410$ A.), which indicates, according to the experiments of Mason[3], that it approaches the magnetite–jacobsite transition field with about the minimum quantity of manganese in solid solution. It may thus be concluded that, while the mineral has just the structure of jacobsite, the composition tends more to that of magnetite and therefore its reactions to etch reagents conform more to magnetite than to jacobsite. This type of jacobsite with composition approaching the magnetite–jacobsite transition field, and exhibiting corresponding etch behaviour, should not be too uncommon in the metamorphic manganese ores of India, of which jacobsite is an important constituent. It may be that such etch characters were overlooked in earlier investigations.

I acknowledge the facilities I enjoyed in the laboratories of the Department of Geological Sciences,

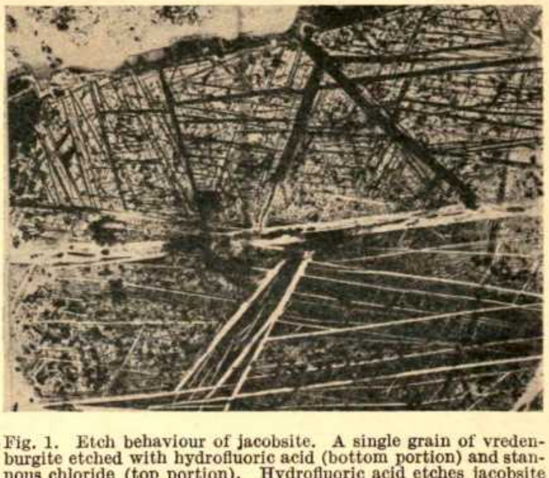

Fig. 1. Etch behaviour of jacobsite. A single grain of vredenburgite etched with hydrofluoric acid (bottom portion) and stannous chloride (top portion). Hydrofluoric acid etches jacobsite sooty black but hausmannite is unaffected. Stannous chloride etches hausmannite but did not attack jacobsite. (× 200)

Jadavpur University, Calcutta, and of the Mineralogy Division, Geological Survey of Canada. I am grateful to Miss J. Trask, of the Geological Survey of Canada, for her help in the X-ray powder analysis of the jacobsites.

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The Spinel–Olivine Inversion in Mg_2GeO_4

DURING the past few years there has been active interest in the problem of alternative explanations other than layers of different composition in the Earth to explain seismic data. The most important of these arises from an early suggestion by Bernal[1] regarding the possible inversion of the orthorhombic mineral olivine to a dense form with the spinel structure. An actual example of this inversion from the spinel to the olivine had been reported by Goldschmidt[2] for the compound Mg_2GeO_4. However, there have always been some doubts regarding this observation, since it was mentioned only in a footnote and could not be repeated.

With the revived interest, there have apparently been several attempts[3] to synthesize the spinel form of Mg_2GeO_4. But the general conclusion was that this form probably does not exist. However, in 1954, Roy and Roy[4] reported the reproducible synthesis and reversible inversion to olivine of a spinel form of Mg_2GeO_4. This work has been generally missed, since the paper describing it was concerned with the morphology of synthetic serpentines. In 1955, a quantitative equilibrium study of the whole problem was started with the view of determining the pressure–temperature conditions for the inversion of natural olivines into spinel structures. The problem was tackled in stages by determining a series of *t–x* sections of the Mg_2SiO_4–Mg_2GeO_4 system; the study of *t–x* sections with 10 and 20 mol. per cent Fe^{2+} replacing Mg^{2+}, and finally a *p–x* section of the Mg_2GeO_4–Mg_2SiO_4 system at 542° C. up to the experimental limit of 65,000 atm. Many of these results were presented orally at the 1956 annual meeting of the Geological Society of America[5]. While the results of this extensive experimental study will be published later elsewhere, it is considered worth while to summarize here the new data on the spinel–olivine inversion obtained from some four hundred runs in hydrostatic or uniaxial pressure devices.

The work utilized high-pressure water as a catalyst, and under such conditions there is no problem with reproducible synthesis of the spinel phase. The inversion temperature for the Mg_2GeO_4 (spinel) $\rightleftarrows$ Mg_2GeO_4 (olivine) equilibrium (obtained by extrapolation from runs as low as 1,000 lb./sq. in.) is 810° C. at atmospheric pressure. The ΔV of inversion from X-ray data is 3·5 cm.^{3}/mol.; ΔH (calculated from the pressure-dependence slope) is 3,690 cal./mol. The entropy of inversion is thus a reasonable 3·4 E.U. The inversion temperature is raised by 0·025 deg. C./bar for the first 5,500 bars. X-ray intensities and infra-red absorption spectra clearly show that Mg_2GeO_4 is an inverse spinel. It may be of interest to record that the inversion in Mg_2SiO_4 as determined by extrapolation of experimental points up to 60 mol. per cent Mg_2SiO_4 in the *p–x* section is set at 100 ± 15 kilobars at 542° C. Further, the change in lattice spacings of the spinel solid solutions of Mg_2GeO_4·Mg_2SiO_4 shows that the spinel form of Mg_2SiO_4 will have a cell edge of 8·22 A. Therefore, the ΔV of this transition is 2·0 cm.^{3}/mol. The dependence of the Mg_2SiO_4 transition upon pressure is beyond direct experimental study at present, but from a consideration of various sections in the *p–t–x* volume constructed with the data for the system Mg_2GeO_4–Mg_2SiO_4, one would expect that it will be only 0·013 deg. C./bar.

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BIOCHEMISTRY

Chlorination of Proteins as a Method of increasing their Opacity in the Electron Microscope

THE basic difficulty in devising a method for selectively increasing the density of protein in a tissue section, in order to increase its contrast under the electron microscope, is to choose some atom or group of atoms unique to the protein, and which may be replaced or substituted by some heavier atom or group. The amide group occurs in all proteins as the peptide link, while it is absent in all other macromolecular cell constituents. N-chlorination(·NH·CO·→ ·NCl·CO·) is a well-known reaction with simple amides, and it therefore seemed that chlorination might offer a simple means of increasing the density of the protein. Although chlorination of other cell constituents (and other structures in the protein) would undoubtedly also occur, it was considered that the background increase in density produced in this way would be small compared with the increase in density of the protein, for theoretically 1 gm. atom of chlorine can react with each 100–150 gm. of protein, depending upon its amino-acid composition. Vandevelde[1] has shown that many proteins, both fibrous and globular, react with chlorine to give materials which contain about 15 per cent chlorine, a content which corresponds to substitution at most of the peptide links. Most of the chlorine is lost from the modified protein by treatment with water, giving hydrochloric acid, which probably arises by hydrolysis of the N—Cl bond followed by oxidation of the protein by the hypochlorous acid which is formed. Exposure to chlorine gas, followed by spraying with iodine and starch solutions, has been used as a delicate test for amino-acid, peptide and protein spots on paper chromatograms[2].

Table 1. CHLORINATION OF VARIOUS PROTEINS BY *tert.* BUTYLHYPOCHLORITE ($((CH_3)_3 \cdot C \cdot OCl)$) IN ANHYDROUS PETROLEUM ETHER

Protein	Gm. protein per gm. atom of chlorine absorbed		
	20 hr.	60 hr.	160 hr.
Native albumin	12,500	4,460	1,057
Alcohol denatured albumin	538	223	132
Fibrin	106	102	100
Keratin	3,570	777	509

We have studied the uptake of chlorine by several dried proteins, suspended in anhydrous solutions of chlorine or *tert.* butylhypochlorite[3] in inert solvents, by estimating the excess active chlorine by iodometry after a given time. The results of a typical experiment are shown in Table 1.

Similar results were obtained with chlorine in dry carbon tetrachloride ; in a number of cases estimation of the chlorine content of the modified protein by the Carius method showed that these figures were essentially correct. Denatured albumin, like the fibrous protein, fibrin, reacted much faster than native albumin, presumably because the disordered peptide chains were more freely accessible to the chlorinating agent. Keratin, in which the structure is additionally stabilized by disulphide cross-links, showed an intermediate reactivity.

In order to test whether a useful increase in contrast under the electron microscope would be observed in protein treated in this way, horse red blood cell erythrocytes were suitable as test objects because they consist largely of protein and are not completely opaque to electrons with accelerating potentials of the order of 75 kV. A bulk preparation of erythrocytes was made by the method of Hillier and Hoffman[4], and after denaturation with alcohol and thorough drying, this material was chlorinated (chlorine in carbon tetrachloride for 24 hr.). The treated erythrocytes contained 11·2 per cent chlorine, and titration of the excess chlorinating agent gave a figure of 206 gm./gm. atom of chlorine absorbed. For electron microscopy, the erythrocytes were deposited directly on an evaporated carbon film mounted on a copper grid, by allowing a small drop of dilute aqueous suspension to evaporate. After immersion in alcohol for several hours, the grids were dried for several days over calcium chloride before they were exposed to dry chlorine gas for 24 hr. Many experiments of this type were made, and under the interference microscope the erythrocytes appeared largely undamaged, provided anhydrous conditions were rigorously maintained. However, under the electron microscope, at a magnification of 10,000–20,000, it was never possible to find a specimen in which the fine structure was not badly disrupted. Frequently a twisted mass of filaments and spirals was observed, and it was consequently impossible to obtain reliable density measurements.

Hydrogen-bonding through the >NH group must necessarily be destroyed by chlorination at the peptide link, and it is this bonding which is thought to be important in maintaining the precise geometry of the folded peptide chains. It is considered that the type of damage observed, together with the rates and extent of chlorine uptake by different types of proteins, is consistent with the view that chlorination at the peptide link occurs with breakdown of hydrogen-bonding between individual amino-acids in the peptide chains, and between peptide chains. If this view is correct, other methods of substitution at the peptide link would also lead to destruction of the protein ultrastructure.

We are indebted to Prof. J. T. Randall and Dr. S. Fritton-Jackson of the Wheatstone Physics Laboratory, King's College, who carried out the electron microscopy. One of us (M. M. C.) wishes to thank the Nuffield Foundation for a research fellowship, during the tenure of which this work was carried out.

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Glucose-*cyclo*-Acetoacetate as a Precursor of Ascorbic Acid in Germinating Green Gram

THAT glucose-*cyclo*-acetoacetate acts as a precursor of ascorbic acid in germinating green gram or mung beans (*Phaseolus radiatus*) has been shown by Nath and his associates[1–3] and confirmed by the use of labelled glucose-*cyclo*-acetoacetate by Thangamani and Sarma[4]. Neither the titrometric indophenol dye method of Bessey and King[5] nor the colorimetric method of Roe and Kuether[6] is specific for L-ascorbic acid. We have therefore used paper chromatography to identify the additional reducing substance formed from glucose-*cyclo*-acetoacetate during the process of germination which decolorizes the indophenol dye, and find it to be L-ascorbic acid.

If glucose-*cyclo*-acetoacetate were a true precursor of ascorbic acid in such a process, the chromatograph would be expected to show greater biosynthesis of ascorbic acid (as indicated by a specific R_F value) on the addition of glucose-*cyclo*-acetoacetate in the germinating medium. The amount of ascorbic acid formed would also be expected to be directly proportional to the amount of glucose-*cyclo*-acetoacetate added.

We adopted the technique of circular paper chromatography used by Nath and Bhattathiry[7] to identify another dienol compound (1 : 2 dienol glucose) in normal blood, and silver nitrate–ammonia was used for staining the chromatogram, as used by Partridge[8] for ascorbic acid.

Chromatograms with a standard ascorbic acid solution and deproteinized extracts of the same weight of seeds germinated for 72 hr. in (*a*) water and (*b*) aqueous solutions of glucose-*cyclo*-acetoacetate, using either 50 mgm./100 seeds or 100 mgm./100 seeds, were obtained. Whatman filter paper No. 1 of 28 cm. diameter fitted with a wick at the central hole was employed, in a Petri dish placed in a closed chamber with a solvent mixture consisting of butanol/acetic acid/water (40 : 10 : 50), the top layer being used. The paper was allowed to dry in air and the staining was done by spraying with a cold solution of silver nitrate–ammonia.

It will be evident from the bands in the chromatogram (Fig. 1) that all of them have the same R_F value, namely, 0·52, which was found to be specific for ascorbic acid by Nath and Bhattathiry[7]. The intensity of the colour of the (G_2) bands with 100 mgm. glucose-*cyclo*-acetoacetate/100 seeds is much greater than that of the (G_1) band with

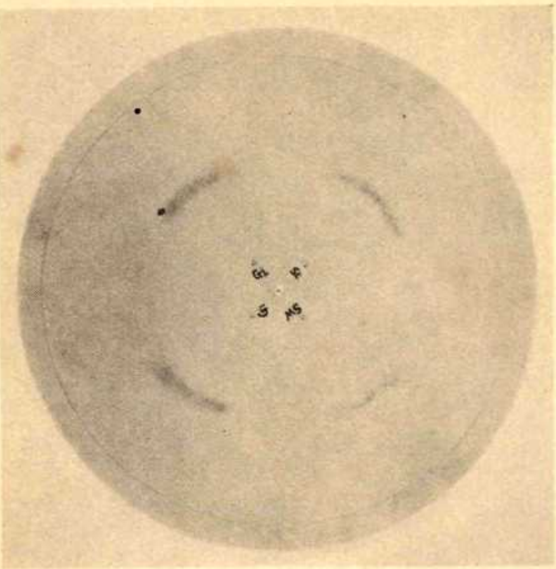

Fig. 1. Circular paper chromatogram showing: *St*, standard ascorbic acid solution; *SW*, aqueous extracts of seeds germinated in water alone; G_1 and G_2, aqueous extracts of seeds germinated with glucose-*cyclo*-acetoacetate (50 mgm. and 100 mgm./100 seeds respectively)

50 mgm. glucose-*cyclo*-acetoacetate/100 seeds, which is again much greater than that (*SW*) with seeds germinated in water only. This confirms that the reducing substance formed from glucose-*cyclo*-acetoacetate during the process of germination of mung beans is ascorbic acid and its biosynthesis varies directly with the amount of glucose-*cyclo*-acetoacetate added.

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PHYSIOLOGY

Antagonism of Choline and Inositol

SIMULTANEOUS administration of choline and inositol to rats prevents the formation of fatty liver to a greater extent than if either substance were given alone[1]. There have also been several isolated reports which suggest to us the existence of an antagonism between choline and inositol. Suppression by choline of the growth of yeast requiring inositol has been reported by Taylor and McKibbin[2]. The addition of choline depressed growth under conditions in which growth was limited by the concentration of inositol in the incubation medium. Also, in studies of renal necrosis found in developing rats fed a diet deficient in choline, Handler[3] observed that the addition of inositol to that diet greatly aggravated the renal necrosis, while it reduced the degree of liver fat in the same animals.

In a study of perosis (slipped tendon) of the developing turkey fed a diet deficient in choline, Jukes[4] observed that dietary inositol cannot relieve the perosis and may even accelerate its appearance. The experiments reported here establish that the addition of inositol to the diet of chicks deficient in choline causes a marked aggravation of perosis, both in rate of appearance and in degree, and that the degree of perosis is intensified by increasing the amount of added dietary inositol (Table 1).

Table 1. EFFECT OF INOSITOL UPON PEROSIS AND GROWTH OF CHOLINE-DEFICIENT CHICKS

Diet	Average perosis score per chick		Average body-weight ± *S.E.* (gm.)	
Added inositol (per cent)	After 2 weeks	After 4 weeks	After 2 weeks	After 4 weeks
0	0·25	2·75	110 ± 3	263 ± 10
0·2	0·88	3·68	116 ± 4	244 ± 19
1·0	1·8	4·5	108 ± 7	224 ± 27

Eight New Hampshire chicks, one day old, were placed on each diet (Table 1) *ad libitum* for four weeks. The basal diet consisted of 'Drackett *C*1' soy protein, 300 gm.; L-cystine, 3 gm.; corn oil, 40 gm.; salts *A*, 60 gm.; crude glucose, 597 gm.; thiamine hydrochloride, 8 mgm.; riboflavin, 8 mgm.; calcium pantothenate, 20 mgm.; nicotinic acid, 100 mgm.; pyridoxine hydrochloride, 8 mgm.; D-biotin, 0·3 mgm.; pteroyl glutamic acid, 3 mgm.; vitamin B_{12}, 0·1 mgm.; vitamin A acetate, 6 mgm.; α-tocopherol, 25 mgm.; α-tocopherol acetate, 25 mgm.; vitamin D_3, 0·02 mgm.; 2-methyl-1,4-naphthoquinone, 1 mgm. The degree of perosis was graded from zero to three by the gross appearance of each leg: maximum severity, designated by a score of 3 for each leg, representing complete loss of the use of the leg.

While the mechanism of the lipotropic action of inositol and choline *in vivo* is still unknown, it is of interest that recent experiments on the biosynthesis of lipids indicate the presence of common intermediates which participate in the formation of inositol- and choline-phosphatides as well as triglycerides[5,6]:

$$\begin{tikzcd}
\text{L-}\alpha\text{-glycerophosphate} \arrow[d, "2\,RCO\text{-CoA}"] & \\
\text{L-}\alpha\text{-phosphatidic acid} \arrow[r, "\text{cytidine nucleotide}", "\text{inositol}"'] \arrow[d] & \text{inositol-phosphatide} \\
\text{D-}\alpha,\beta\text{-diglyceride} \arrow[r, "CDP\text{-choline}"] \arrow[d, "RCO\text{-CoA}"] & \text{lecithin} \\
\text{triglyceride} &
\end{tikzcd}$$

This scheme suggests that either choline or inositol might exert a lipotropic effect by stimulating formation of the corresponding phosphatide, in which form fatty acids are perhaps more soluble or are otherwise made more accessible to further metabolism than they are in the form of triglycerides.

On the other hand, during periods of rapid synthesis of cells, such as the growth of a young animal, it is likely that specific phosphatides are required for the formation of cellular and subcellular constituents and that for this purpose inositol and choline are not interchangeable.

Thus there is evidence suggesting synergism between inositol and choline from experiments related to lipotropic action, and there is also evidence of antagonism in experiments related to growth. This paradox may be explained by present knowledge at the enzyme-level. The synergistic lipotropic action may be related to a shunt of precursors away from triglyceride formation by either inositol or choline, while the antagonism may be related to depression of the formation of a particular structural phosphatide by the precursor of another, for example, lecithin, by inositol under conditions in which low levels of choline are present.

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Sodium, Potassium, Calcium and Chloride Ion Contents and Protein Fractions in the Fluids of Chick Embryos

Among substances present in the amniotic fluid, the protein fractions and mineral components preserving osmotic equilibrium between the amnion and the growing embryo itself are especially significant for the development of the embryo.

In the present investigation, the amniotic fluid from incubated hen's eggs was used and for comparison the allantoic fluid and the rest protein of fertile eggs between the tenth and seventeenth days of incubation. For this purpose, a culture of embryos was grown at the Institute of Medical Microbiology of the Medical Academy at Poznań. The amniotic and allantoic fluids were extracted with an aseptic needle and syringe after breaking the egg shell, and were transferred to corked aseptic tubes. Protein from incubated eggs was placed in weighed test-tubes containing a physiological salt solution or buffer solution necessary for electrophoretical investigations. The fluids and protein were kept in a refrigerator until used in experiments.

The level of sodium, potassium and calcium ions in the amniotic and allantoic fluids was determined with a flame photometer (Zeiss, Jena), and their contents expressed in milliequivalents. The chloride ion content was determined by Volhard's method and also expressed in milliequivalents. The total protein content was examined by the biuret method[1], using a Coleman spectrophotometer. The protein fractions of both fluids and the rest protein were separated by free electrophoresis ('Fokal' *F* apparatus, constructed according to Arne Tiselius by Strübin, Basle). For obtaining protein diagrams the following buffer solution was used: veronal sodium salt, 5·88 gm.; sodium acetate ($CH_3COONa.3H_2O$), 3·88 gm.; potassium oxalate ($(COOK)_2.2H_2O$). 1·38 gm.; hydrochloric acid 0·1 *N* (HCl), 20·00 ml.; distilled water to 1 litre. Such a solution has *p*H 8·9, and ionic strength μ 0·1. Before electrophoresis, the amniotic and allantoic fluids of low protein contents were condensed *in vacuo* over phosphorus pentoxide to a concentration of 1 per cent protein.

Table 1. Mean Ion Contents (in m.equiv.) of the Amniotic and Allantoic Fluids of Normally Developing Chick Embryo

Ions	Days of life							
	10	11	12	13	14	15	16	17
	Amniotic fluid							
Na^+	127	134	130	132	112	107	119	118
K^+	4·1	4·5	4·7	7·0	21·8	23·8	19·2	18·0
Ca^{2+}	—	1·6	2·1	3·5	4·7	3·6	—	3·2
Cl^-	—	131	141	144	108	—	—	—
	Allantoic fluid							
Na^+	—	115	110	105	84	82	—	—
K^+	—	12·0	13·0	20·0	25·0	26·0	—	—
Ca^{2+}	—	3·5	2·0	2·4	1·5	2·0	—	—
Cl^-	—	68	90	84	72	—	—	—

The results of measurements of the concentration of mineral components in both fluids of the growing chick embryo, undergoing normal development between the tenth and seventeenth day of its life, are shown in Table 1.

In physiological conditions, the concentrations of sodium and chloride ions in the amniotic fluid drop as the embryo develops, that is, as incubation proceeds; starting from the thirteenth or fourteenth day of the life of the embryo, the level of potassium ion rises to 4–5 times its value in the earlier days. The allantoic fluid was found to undergo analogous changes in ion content; however, the potassium ion has originally a higher concentration here than in the amniotic fluid. The sodium and calcium ions have lower concentrations in the allantoic fluid than in the amniotic fluid.

The present results differ from those of Kamei[2], obtained in 1927, especially with regard to sodium, potassium and calcium ion determinations in both fluids. The fact that Kamei obtained higher values for these ions is probably due to his use of gravimetric methods: sodium and potassium were weighed as chloride, potassium was estimated separately as potassium chloroplatinate (K_2PtCl_6) and the sodium ion level determined by subtraction. Kamei's results for chloride generally coincide with the present results, though they are somewhat higher. It is also possible that the discrepancy arises from some differences in the races of hens used for investigation.

Daily control of the levels of ions made it possible to detect differences in the level of potassium ions between the twelfth, thirteenth and fourteenth days of the embryo in both fluids. This was not noticed by Kamei, whose measurements date from the ninth and fourteenth day.

Simultaneously with the rise in content of potassium ions in the amniotic fluid, the protein content undergoes a marked change on the thirteenth or fourteenth day of the life of the embryo. In fact, determinations of the total protein showed the amniotic fluid to be poor in protein during the eleventh to thirteenth days of embryonic development, when the protein concentration amounts to no more than 0·5 gm. per 100 ml. of the fluid. On the other hand, the amniotic fluid of an embryo more than 14 days old is highly proteinous, containing 9–10 gm. of protein per 100 ml. of the fluid.

The amniotic fluid of low protein content, on being concentrated *in vacuo*, showed three fractions on the electrophoretic diagram. That with the greatest velocity contains about 98 per cent of the total amount of protein, the two remaining fractions containing but 1 per cent each (Fig. 1*a*). Allantoic fluid of low protein content exhibited a similar electrophoretic diagram.

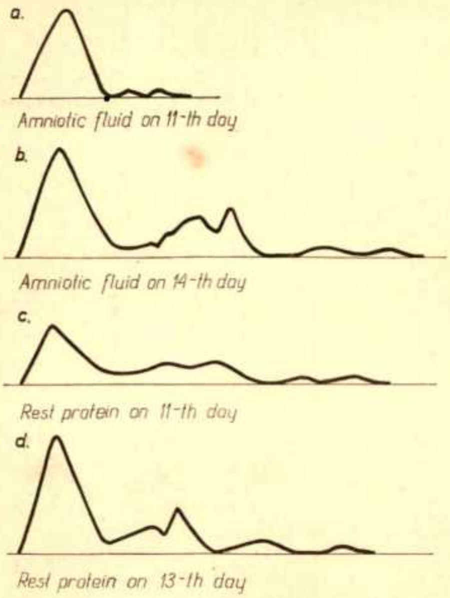

Fig. 1. Electrophoretic diagrams obtained in free electrophoresis in 'Fokal' *F* apparatus

The highly proteinous amniotic fluid of the fourteenth day contains five electrophoretically distinct fractions (Fig. 1*b*). The largest, amounting to 62 per cent of the total protein, presents a broad base in the diagram, which proves it to be inhomogeneous. The second, third and fourth fractions amount respectively to about 17, 10 and 8 per cent of the total protein. The latter fraction, in the buffer solution used, moves towards the cathode, and amounts to about 3 per cent of the total protein. The rest protein of incubated eggs on the eleventh and thirteenth days exhibited similar electrophoretic diagrams (Fig. 1*c* and *d*); the diagram on the eleventh day shows weakly developed gradients.

The similarity of the diagrams obtained with highly proteinous amniotic fluid and that of the rest protein of the incubated egg on its thirteenth day is noteworthy (Fig. 1*b* and *d*). It had already been observed by M. E. Marshall[3] in the amniotic fluid of the incubated egg and the protein from newly laid egg.

The biochemical changes in the composition of the amniotic fluid and in the amount of total protein, between the twelfth and fourteenth days of the life of the embryo, observed as a stepwise variation in the potassium ion and total protein contents and as variations in the electrophoretically separated protein fractions, are probably caused by the serum–amniotic junction.

I am indebted to Prof. Jan Adamski (Institute of Medical Microbiology, Medical Academy, Poznań) for the material received for investigation, and to Prof. Jan Roguski (IInd Clinic of Internal Medicine, Medical Academy, Poznań) for permission to carry out the electrophoretic analysis in his laboratory.

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Demonstration of Small Components in Red Cell Hæmolysates by Starch-gel Electrophoresis

STARCH-GEL electrophoresis[1] has been used successfully for the investigation of human and animal sera; it is superior to other methods because it affords greater resolution and ability to demonstrate small components. The same method has also been applied to the study of human hæmoglobin, although the results reported so far[2-4] have not provided information different from that obtainable by other electrophoretic techniques.

We have used this supporting medium with phosphate buffer (pH 6·5, $\Gamma/2$ 0·033) in the electrode vessels and for the preparation of the gels (12 gm./100 ml. of hydrolysed starch, Connaught Laboratories, Toronto). The hæmoglobin solution (10–15 gm./100 ml.) is introduced into suitable slits either on a double piece of filter paper (Whatman 3*MM*) or as a paste moulded with unboiled starch. Direct current at 280 V. and 26 m.amp. is applied for 6–8 hr. to two plastic trays, each measuring 250 mm. × 60 mm. × 6·5 mm. After completion of the run one of the cut surfaces is stained for protein[1] and the other is treated with a benzidine reagent[2]; the concentration of hydrogen peroxide in the latter is preferably kept low (1–3 per mille) in order to avoid distortion of the gel by catalase activity.

A coloured zone at the position of hæmoglobin *A* is still demonstrable with benzidine when the hæmoglobin solution applied has been diluted to 1 part in 2,000, and with amidoschwartz at a dilution of 1 part in 500. The electrophoretic pattern appears similar whether the hæmolysate is freed of stromal material by extraction with toluene, by precipitation with phosphate buffer (0·3 *M*, pH 6·8) or by high-speed centrifugation. For the identification of some zones a two-dimensional technique[5] has been applied (paper electrophoresis at pH 8·6 or 6·7, followed by starch-gel electrophoresis at pH 6·5 of segments cut longitudinally to the direction of migration).

Under the above conditions the normal hæmoglobins A_2, *F* and *A* move in that order a short distance toward the cathode, hæmoglobin *F* not separating from *A*; all other fractions migrate away from the point of insertion to the anode. By protein stain the following zones can regularly be observed (Fig. 1):

Zone 1, placed immediately after the slit of insertion, benzidine negative, is always present in adults, but is absent or only barely visible in cord blood; it corresponds to a protein which on paper, starch-

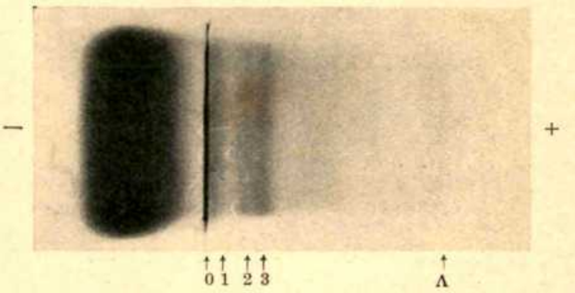

Fig. 1. Starch-gel electrophoresis of red cell hæmolysate from adult blood, 6 hr., amidoschwarz stain. 0, application slit. Numbers and letters correspond to zones described in text. The weaker fractions ahead of band Λ are not reproduced on the photograph

block and starch-gel electrophoresis at pH 8·6 migrates slightly more slowly than A_2.

Zone 2 is a narrow band, which probably corresponds to catalase, because oxygen is liberated only in this area ; at low concentrations of hydrogen peroxide a thin benzidine-positive line appears in this region.

Zone 3, closely following 2, is very prominent and occurs in both adult and cord blood. It is followed by a number (usually 3–4) of weak and less sharply delineated bands, which have not been identified.

The zone designated Λ occupies the same position as serum albumin ; in the presence of traces of serum in the hæmolysate this band stains more intensely and, at times, may also be demonstrated by the benzidine reagent as a weak line. This observation suggests binding of hæmoglobin or its derivatives by albumin. A zone with similar properties is also demonstrable on starch gels used with borate buffer, pH 8·4 ; in both buffers it is of definitely higher anodic mobility than hæmoglobin H (Fig. 2). The characteristics of this zone are reminiscent of the small fraction V observed by Huisman and Martis in many samples by chromatography on carboxymethylcellulose[6].

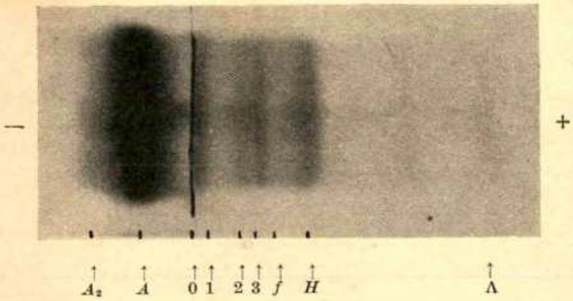

Fig. 2. Electrophoresis of hæmoglobin from an adult with hæmoglobin H, 8 hr., amidoschwarz stain. Symbols as for Fig. 1; f indicates relative position of 'fast' fœtal hæmoglobin

Three further very weak zones, not identified, precede band Λ towards the anode.

By means of the benzidine reagent we were able to demonstrate in all samples of cord blood a well-defined zone with peroxidase activity, situated only slightly ahead of zone 3 (Fig. 3) ; it is estimated to amount to 0·5–1 per cent of the total hæmoglobin. The position of this band, as well as evidence obtained by the two-dimensional technique, strongly suggest that it corresponds to a 'fast' fœtal hæmoglobin, increased levels of which have been observed in several cases by paper electrophoresis (ref. 7 and Vella, F., and Lie-Injo Luan Eng, personal communications and unpublished results). This zone has not been found in adults ; however, minimal amounts were detected in four adults with hereditary anæmias and increased levels of hæmoglobin F (12–20 per cent). Conversely, this same fraction was definitely present in four cases presenting hæmoglobin H—which is of higher anodic mobility—and a minimal increase of the alkali-resistant pigment.

For the separation of certain hæmoglobin variants and of components which at alkaline pH move slower than A (such as hæmoglobin A_2, the protein of zone 1 and a further red cell protein), borate buffer at pH 8·4[1] or *tris* buffer[8] are preferable to the phosphate used here ; hæmoglobin H, the 'fast' fœtal fraction and zone Λ can also be demonstrated in borate buffer. However, the delineation of components with a higher anodic mobility than hæmoglobin A is generally superior in phosphate. Furthermore, under the above conditions, the mobility of the zones is not affected by their relative concentration.

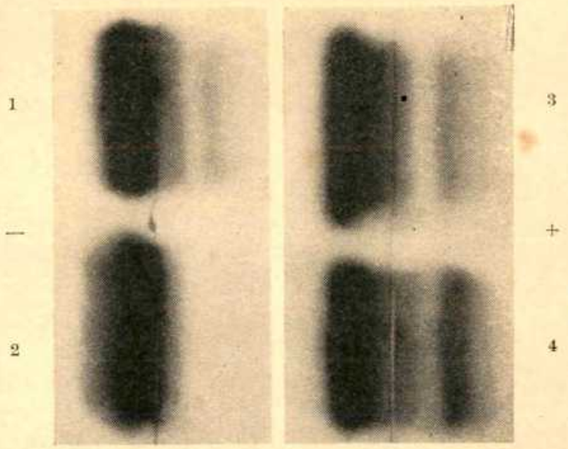

Fig. 3. Comparison of (1) normal cord blood hæmoglobin with (2) normal adult hæmoglobin, and (3) hæmoglobin from cord blood of a 6 months premature infant with (4) cord blood presenting a very high percentage of the fast fœtal fraction. Starch gel electrophoresis for 6 hr., treated with benzidine reagent

It is believed that this method, although not yet suitable for accurate, quantitative use, has the advantage of clearly demonstrating minor components of red cell hæmolysates, not well shown by other electrophoretic procedures. Work on the nature of the zones observed and their alterations in various conditions is in progress.

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Distribution of Alkaline Phosphatase in the Arteries of Several Species

A CHANCE observation in our laboratory led us to study the activity of the alkaline non-specific monoesterase in the arterial wall. The distribution of this enzyme within the arteries has received but scant attention and contradictory reports appear in the literature. Kay[1] states that none is found when chemical methods are used, whereas Gomori[2], using a histochemical technique, reports that the enzyme is found in the adventitia of medium-sized arteries. In the human being, no activity has been found[3] chemically in the aorta at an alkaline pH, or only traces found in this vessel and in other arteries[4] ; on the other hand, the enzyme has been demonstrated histochemically in early atheromatous plaques[5] as well as chemically in peripheral arteries[6].

The present observations show that the activity of alkaline phosphatase is not uniform and that there are differences between arterial territories as well as between species; it seems possible that conflicting reports may be due to this fact. Furthermore, an interesting and unexplained fact has been disclosed, namely, an apparent inverse relationship between the enzyme activity and the ability of several species to develop atherosclerosis induced by cholesterol.

Rabbits, chickens and rats were anæsthetized with sodium pentobarbital, blood collected and the arterial system perfused with saline in order to avoid contamination with blood. The aorta and the cerebral vessels (free from the choroid plexus) were removed, blotted with filter paper and weighed; they were then frozen and cut into 10μ sections with a microtome, homogenized and the enzyme activity in approximately 20 mgm. of tissue determined by the method described by Kaplan and Narahara for blood serum[7]. Incubation was carried out at 37° C. for 30 min. with disodium phenylphosphate as substrate, and with sodium borate buffer at *p*H 9·4. The enzyme was also determined in citrated plasma.

The results, expressed in μmoles of phenol liberated under the stated conditions, are shown in Table 1. It can be seen that the alkaline phosphatase activity is similar in the plasma of rabbits (50·1 ± 7·17 μmoles/ml., mean ± standard error) and rats (60·9 ± 4·40) whereas it is much higher in chickens (303·0 ± 24·7). In the aorta, however, the activity was very low in rabbits (0·06 ± 0·006) and in chickens (0·14 ± 0·018), while it was 0·48 ± 0·028 in the rat. In the cerebral vessels it was strikingly higher and also different in the three species (0·21, 2·74 and 1·10, in the rabbit, rat and chicken respectively). It must thus be concluded that the alkaline phosphatase content of the vessels is not the same in different species, that plasma values bear no relationship to the arterial activity and that the cerebral vessels have a much greater enzymatic concentration than the aorta.

Table 1. ALKALINE PHOSPHATASE ACTIVITY IN SEVERAL SPECIES (IN μMOLES OF PHENOL LIBERATED UNDER STANDARDIZED CONDITIONS; MEAN ± STANDARD ERROR)

Animal	Plasma (per ml.)	Aorta (per mgm. of wet tissue)	Cerebral vessels (per mgm. of wet tissue)
Rabbit	(18) 50·1 ± 7·17	(14) 0·06 ± 0·006	0·21*
Rat	(12) 60·9 ± 4·40	(16) 0·48 ± 0·028	2·74†
Chicken	(10) 303·0 ± 24·7	(10) 0·14 ± 0·018	1·10†

All determinations were carried out in duplicate; figures in parentheses, number of animals.

* Six determinations on pools of three animals.

† Two determinations on pools of six animals.

Although very little is known about the chemical reactions which might be catalysed by alkaline phosphatase in the arterial wall, the changes that the enzyme might undergo in different circumstances seem to be worthy of study. Finally, it is also of interest in connexion with the problem of atherosclerosis, that in rabbits and chickens atherosclerosis is easily induced by cholesterol[8], and they have very little alkaline phosphatase in the aorta, whereas rats show a high enzymatic activity and very rarely develop the disease[9]; furthermore, cerebral lesions are not seen even in atheromatous rabbits which have been fed cholesterol[10] and, as was shown, the cerebral vessels possess a high alkaline phosphatase activity. Further work on these apparent relationships is clearly needed and is being undertaken in our laboratory. Results will be published in more detail elsewhere.

We are grateful to Prof. Eduardo Braun Menendez for helpful suggestions and criticisms.

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A Germination Inhibitor and Root-Growth Retarder in Chou Moellier (*Brassica oleracea* var.)

INVESTIGATIONS are being undertaken at this Station into local problems associated with the establishment of new pastures. Such pastures are commonly sown in the autumn following a summer crop of chou moellier (marrow stem kale), *Brassica oleracea* var. A frequent outcome of such sowings is that the grass components of the seeds mixture germinate and grow apparently normally, while the legume component may or may not germinate. If the seeds of the legume component (chiefly white clover) do germinate, and seedlings emerge, they frequently die off in four to six weeks.

In the course of *in vitro* studies undertaken to throw light on this problem of clover seedling mortality the presence of a germination inhibitor in chou moellier has been demonstrated. A technique has been used in which ten white clover (*Trifolium repens*) seeds are sown on a filter paper in a Petri dish, while on a second filter paper slightly overlapping the first are placed sections of chou roots, stems or leaves, or finely minced parts of these organs. The seeds are then provided with sufficient moisture for germination by applying water to the chou plant material and allowing it to pass to the seeds across the bridge formed by the overlapping filter papers.

The germination in eight days of white clover seeds has been reduced from 87 per cent in the controls to 10 per cent where minced chou roots were present on the adjacent filter paper, with lesser reductions in germination where minced stems and leaves and unminced sections of the roots were present.

The inhibitory effect appears to be irreversible, since ungerminated seeds removed after eight days from the presence of chou roots, leaves and stems to clean filter paper in Petri dishes uncontaminated by chou plant material and watered with distilled water failed to germinate after a further ten days.

In the few cases where clover seeds were able to germinate in the presence of chou moellier roots, the seedling radicles became blackened at the tip, root hairs were very sparse by comparison with the control seedlings, and within three weeks the seedlings adjacent to the chou roots had all died.

Evaluation of the part played by the inhibitor in the field mortality of clover seedlings awaits the result of field trials now in progress.

The effect of the inhibitor has also been studied in relation to germination and subsequent growth of perennial ryegrass (*Lolium perenne*) and New Zealand short rotation ryegrass (*L. perenne* × *L. multiflorum*). With neither species did the presence of chou roots, leaves or stems reduce germination percentage. However, using the technique outlined above for clovers, the presence of sections of chou roots on the adjacent filter paper had a most striking effect on the total root length per rye-grass seedling. The mean root lengths in millimetres, for 30 seedlings in each case, are given in Table 1.

Table 1

	Controls	With chou roots
Perennial rye-grass	24 mm.	5 mm.
Short rotation rye-grass	26 mm.	1 mm.

Later observations suggest that parts of the swede turnip plant and of the common weed spurrey (*Spergula arvensis*) may have similar effects.

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Enzymic Nature of the Serum Globulin Permeability Factor

The globulin permeability factors obtainable from the serum of man[1], guinea pig[2,3], rat[4] and rabbit[4] appear to be proteases because they are highly active on vascular endothelium—on a molar basis, they are 60–2,000 times as active as histamine, itself a potent permeability factor[5]; and because they are readily inhibited by prior treatment *in vitro* with the trypsin inhibitors from soya bean, lima bean and bovine pancreas. The action of these inhibitors, however, is apparently very rapid, a mixture of factor and inhibitor only 1 min. old being inactive when injected into the skin of animals with circulating pontamine blue[4,7]. Consequently, it is impossible to distinguish inactivation of a protease permeability factor *in vitro* from inactivation of a protease newly activated *in vivo*. Moreover, even the best preparations of permeability factors also contain known serum proteases, and so far no enzyme substrate has been found which is hydrolysed by serum fractions in strict proportion to their content of permeability factor.

The enzymic nature of the factors was more firmly established when one of us (E. L. B.[6]) demonstrated that guinea pig permeability globulin was irreversibly inactivated by prior treatment *in vitro* with di*iso*propyl phosphofluoridate and subsequent dialysis to remove excess di*iso*propyl phosphofluoridate. Thus, treatment with $4\cdot4 \times 10^{-4}$ *M* di*iso*propyl phosphofluoridate for 2 hr. at 37° completely inactivates 54 'effective blueing doses' (EBD)[7]. Since the inactivation *in vitro* (Table 1) is slow and progressive, the drug cannot be suppressing a protease activated *in vivo*. Furthermore, the minimally effective concentration of di*iso*propyl phosphofluoridate for inactivation at 37° C. for 1 hr. is of the order of 10^{-5} *M*, a concentration like that inactivating trypsin, in contrast to concentrations of 10^{-8}–10^{-9} *M* effective on enzymes with a more restricted esterase activity[8], for example, choline esterase.

Table 1. PROGRESSIVE INHIBITION OF PERMEABILITY-INCREASING POTENCY OF GUINEA PIG FACTOR BY PRIOR TREATMENT *in vitro* WITH DI*iso*PROPYL PHOSPHOFLUORIDATE (DFP)

Amt. factor (EBD)	Concn. DFP (*M*)	Percentage inhibition after treatment with DFP for			
		½ hr.	1 hr.	2 hr.	6 hr.
2	$3\cdot3 \times 10^{-6}$	*nt*	*nt*	33	39
2	1×10^{-5}	39	59	75	75
6	1×10^{-5}	*nt*	48	89	92
6	$3\cdot3 \times 10^{-5}$	50	63	82	98
18	1×10^{-4}	39	83	96	100

EBD, Effective blueing dose; *nt*, not tested.

Nevertheless, the factors in guinea pig and rat serum, if they are enzymes, appear to attack ester linkages. Thus 0·01 *M* of both *p*-toluene sulphonyl L-arginine methyl ester and of benzoyl L-arginine methyl ester prevent inactivation of the guinea pig factor by $2\cdot5 \times 10^{-4}$ *M* di*iso*propyl phosphofluoridate. The ethyl esters of L-leucine, L-lysine, L-phenylalanine, DL-serine, L-tyrosine and acetyl L-tyrosine were ineffective in concentrations of 0·01 *M*. Rat factor is also protected by *p*-toluene sulphonyl L-arginine methyl ester, 0·003 *M* successfully competing with 10^{-3} *M* di*iso*propyl phosphofluoridate. These facts are compatible with the serum factors being proteolytic enzymes with an active site similar to that of trypsin. They are distinguished from trypsin by their insusceptibility to the trypsin inhibitor in ovomucoid[9]. The direct competitive inhibition of the factor by these synthetic amino-acid esters cannot be satisfactorily tested *in vivo* because they are themselves fairly potent permeability factors.

When partially purified preparations of guinea pig factor were fractionated on an N,N-diethylaminoethyl–cellulose column the permeability factor activity was associated with a soya bean inhibitable esterase with a *p*H optimum around 9·0. Treatment of cell-free guinea pig serum with glass particles, which activates the permeability factor[10], also activates a soya bean inhibitable esterase with a *p*H optimum around 9.

Under standard conditions, a fixed dose of di*iso*propyl phosphofluoridate has a remarkably similar effect on the permeability factors from guinea pig, rat and rabbit whether they are tested in the corresponding homologous animal or in either of the two heterologous animals. Prior treatment *in vitro* with 10^{-4} *M* di*iso*propyl phosphofluoridate for 60 min. at 37° C. decreases the permeability-increasing potency in all cases by a factor of about 3, the extreme values being 1·8 and 4·4. It is of interest that the esterase inhibitors[8] diethyl *p*-nitrophenyl phosphate (*E* 600), tetraethyl pyrophosphate and *bis*-mono*iso*propyl aminofluorophosphine oxide, in concentrations up to 3×10^{-4} *M*, do not inactivate the factors, though tetraethyl pyrophosphate has a slight effect at 3×10^{-3} *M*. Systemic tri-O-cresyl phosphate is converted in the liver into an inhibitor of serum and liver aliesterases[11]; when given 4 and 24 hr. previously in the rat, it did not substantially inhibit the permeability effect of histamine, 5-hydroxytryptamine, the histamine-liberating compound 48/80 or rat-serum factor.

The use of di*iso*propyl phosphofluoridate has enabled us to establish more firmly the hypothesis that the globulin permeability factors are proteases. The drug is also useful for distinguishing the permeability effects of the globulin from those of other endogenous factors. Di*iso*propyl phosphofluoridate has no *in vitro* effect on histamine, tested in all three species of animal, or on compound 48/80 and 5-hydroxytryptamine, tested in the rat. But its use as an *in vivo* reagent for identifying effects due to the globulin factors is limited by its toxicity in concentrations that might be expected to inactivate proteases. Thus, 0·1 ml. of 10^{-4} *M* di*iso*propyl phosphofluoridate given intracutaneously is sufficient to induce local fibrillation in the muscles of the skin. Given systemically, di*iso*propyl phosphofluoridate is likely to be even less useful for this purpose, because in non-toxic doses it will effect mainly the numerous esterases of the body susceptible to concentrations of the order of 10^{-8}–10^{-9} *M*.

In contradistinction to the observations of Spector and Willoughby[12] in the rat, in our hands only obviously toxic doses of systemic di*iso*propyl phosphofluoridate decreased the action of globulin permeability factors injected intracutaneously in both rats and guinea pigs. In any event, the action of the globulin factors is not exclusively affected, since the permeability effects of histamine, compound 48/80 and 5-hydroxytryptamine in rats and guinea pigs are depressed to the same extent.

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Equilibration of Labelled Magnesium between Sheep Plasma and Red Cells

The following work was undertaken to determine the rate of transfer of magnesium across the sheep erythrocyte membrane held in a stable *in vitro* system. It is considered that such information should be of value in the elucidation of the etiology of hypomagnesæmia.

Samples of heparinized sheep blood, to which a known percentage of isotonic glucose containing carrier-free magnesium-28 had been added, were incubated for different periods at 40° C. During this incubation frequent aeration with a water-saturated gaseous mixture of 5 per cent carbon dioxide and 95 per cent oxygen was carried out. A layer of paraffin above the blood prevented the interchange of gases between the blood and its environment except during aeration. After each relevant period the particular sample was centrifuged under paraffin, *p*H measured and the plasma and erythrocytes separated. The magnesium-28 was counted in each sample and its total magnesium estimated chemically by way of ammonium vanadate (Rook, J. A. F., private communication).

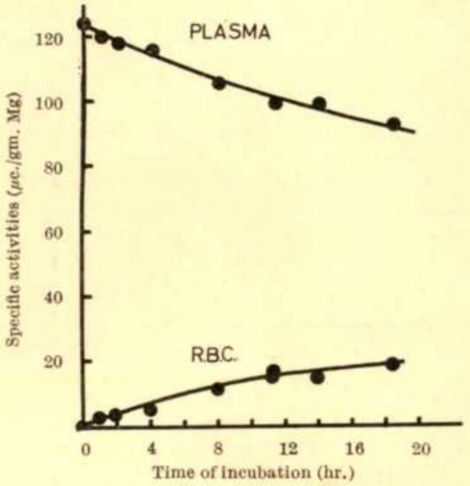

Fig. 1. Magnesium-28 exchange between plasma and red cells of sheep blood

The changes with time of the specific activities of the plasma and erythrocyte magnesium were determined (Fig. 1). The rate of transfer of magnesium between the extracellular and intracellular compartments was calculated by the method used for potassium exchange[1]. It amounted to 3·4 per cent of the plasma magnesium content per hour.

In order to investigate any effect exerted by *p*H on this magnesium transport, the above experiment was repeated at different blood *p*H's. The results showed no significant effect of *p*H on the rate of transport of magnesium between plasma and erythrocytes *in vitro* over the *p*H range studied (7·26–8·07).

The above work, in detail, along with its extension to *in vivo* experiments with sheep, will be published shortly elsewhere.

We wish to record our appreciation for the financial assistance afforded us by the Secretary of State for Scotland and by the Animal Health Trust to one of us (A. D. C.).

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Detection of Carriers in Hereditary Galactosæmia

ATTEMPTS are being made[1] to detect the heterozygous state for galactosæmia by means of the uridine diphosphoglucose consumption test on erythrocytes —a test devised by us for the detection of galactosæmia[2]. This test was designed so as to give a maximum of difference between normal persons and persons having congenital galactosæmia, in which no galactose-1-phosphate uridyl transferase is discernible in erythrocytes[3,4]. In order to magnify this difference and hence provide an unambiguous proof for the clinician[2,3] this reaction mixture is over-incubated. With near-normal activities, the reaction is brought close to the equilibrium point (cf. refs. 2, 4, 5), and the rates measured are obviously not maximum rates. Experiments in which aliquots for uridine diphosphoglucose determination were taken at 5, 10 and 20 min. incubation time designed to give a quantitative expression of maximum rates have also been carried out[5]. In this work we used the consumption as well as the combined epimerase test[2,3], and yet, only in about two-thirds of the specimens did we succeed in obtaining linearity between incubation time and conversion. Accordingly, we believe it even less likely that the unmodified clinical consumption test (in which only one aliquot at 30 min. incubation is drawn) should be able to detect heterozygous carriers. Therefore, as stated previously[2,6], we do not recommend the consumption test for the latter purpose.

This is not to deny the high degree of reliability of the consumption test and especially our combined test[2,3] for detecting homozygous individuals afflicted with galactosæmia. Not only has the test proved to be reliable and specific, but it also circumvents the loading of afflicted infants with galactose. Moreover, as suggested by Dr. H. N. Kirkman[7], a slight modification of the test may prove useful in spotting galactose-1-phosphate in blood and hence turn attention toward possible faulty diets in case of galactosæmia[7].

We have pointed out on earlier occasions[2,6] that in order to develop reliable techniques for detecting heterozygous carriers in galactosæmia it is necessary to develop methods in which it is possible to obtain accurate and abundant results under conditions in which one can expect maximum rates for galactose-1-phosphate uridyl transferase. Such methods, which were developed more than a year ago by Dr. Kirkman[8], permit the recording of 20–25 points during the period in which the reaction is proceeding at maximum rate. The first results, which were reported some time ago[9], showed that the parents of galactosæmic children frequently manifest partial defects in the above-mentioned enzyme. In a more detailed publication[8] Kirkman evaluates the method and the results. It seems that this method permits the detection of an enzyme defect in the great majority of carriers of hereditary galactosæmia.

Note added in proof : A paper dealing with galactosæmia carriers has recently appeared (Brettauer *et al.*, *Proc. U.S. Nat. Acad. Sci.*, **45**, 328 ; 1959) which describes preliminary results obtained with a similar modification of our diagnostic methods[2], namely, shorter incubation time and higher substrate concentrations. Values for transferase activity in hæmolysates ranging between 4·8 and 8·1 μmoles/hr./gm. cells are reported. In a smaller survey I found values ranging between 4·0 and 5·8 μmoles/hr./gm. (unpublished work).

We also agree with Brettauer *et al.* that the modified diagnostic method makes it possible to find markedly lower enzyme values in hæmolysates from parents of galactosæmic children. I have found values as slow as 1·2–2·2 μmoles/hr./gm. cells. In spite of these differences we cannot recommend the "one point method" for use in the diagnosis of individual carriers. The manometric method as described by Kirkman gives a guarantee that one is really dealing with zero-order kinetics and we believe that at the present time it is the only test which can be used in the diagnosis of carriers in families in which galactosæmia has not been observed before. A detailed discussion of these problems will be given elsewhere.

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Gene Action in Erythrocyte Deficiency of Glucose-6-phosphate Dehydrogenase : Tissue Enzyme-Levels

THE susceptibility to increased hæmolysis following ingestion of such agents as primaquine, naphthaline, nitrofurans, other drugs and the fava bean is associated with intrinsic defects in erythrocyte metabolism. These defects include a lower concentration of reduced glutathione[1], instability of reduced glutathione during incubation of the cells with acetylphenylhydrazine[2], and a deficiency in glucose-6-phosphate dehydrogenase[3]. Recent studies have suggested that this erythrocyte enzymatic deficiency is genetically determined, and inherited as a sex-linked characteristic of intermediate dominance[4–6].

In this investigation, it has been found that subjects with an erythrocyte deficiency of glucose-6-phosphate dehydrogenase have normal levels of this enzyme in their leucocytes. In addition, two subjects with markedly deficient erythrocyte glucose-6-phosphate dehydrogenase did not have a similarly decreased level of this enzyme in their liver.

Leucocytes were separated from venous blood by a method of dextran flotation which yields a white blood cell preparation contaminated with fewer than 5 red cells for each leucocyte[7]. This degree of contamination by red cells does not affect the assays of leucocyte enzyme. The leucocytes were suspended in approximately 20 vol. of isotonic potassium chloride buffered at pH 7·4 and disrupted by freezing and thawing three times. Leucocyte counts were performed prior to, and following, this procedure to ensure that assays were performed only on samples in which more than 90 per cent of the white blood cells were destroyed. Liver tissue was obtained by surgical biopsy through an abdominal incision. This tissue was homogenized and resuspended in isotonic potassium chloride buffered at pH 7·4. The erythrocytes were prepared as previously described[8]. Glucose-6-phosphate dehydrogenase, 6-phosphogluconic dehydrogenase and purine nucleoside phosphorylase were assayed by techniques described elsewhere[8].

In subjects whose red cells were markedly deficient in glucose-6-phosphate dehydrogenase, the leucocyte content of this enzyme was not significantly different from that in leucocytes of the control group (Table 1). Glucose-6-phosphate dehydrogenase activity was markedly higher (on a per 10^9 cell basis) in leucocytes than in erythrocytes. No significant differences were found in purine nucleoside phosphorylase activity of leucocytes or of erythrocytes of control subjects compared with persons with red cells deficient in glucose-6-phosphate dehydrogenase.

Table 1. GLUCOSE-6-PHOSPHATE DEHYDROGENASE ACTIVITY IN LEUCOCYTES AND RED CELLS OF CONTROL SUBJECTS AND PERSONS WITH A DEFICIENCY OF THIS ENZYME IN THEIR CIRCULATING ERYTHROCYTES

Subjects	Number	Leucocytes*	Red cells
Control	31	37·3 ± 5·8	0·49 ± 0·11
Deficient red cell *G-6-P.D.*†	14	36·8 ± 1·8	0·07 ± 0·01

* The unit of enzyme activity is expressed as the change in optical density per min. per 10^9 cells (△ opt. dens./min./10^9 cells). The mean values + or − one standard deviation are given.

† *G-6-P.D.*, glucose-6-phosphate dehydrogenase. All subjects included in this group had erythrocyte glucose-6-phosphate dehydrogenase levels below three standard deviations of the mean for the control group.

In 4 control subjects the level of glucose-6-phosphate dehydrogenase in liver was 0·081, 0·060, 0·58 and 0·088 units (change in optical density units per min. per mgm. liver nitrogen), respectively. Two subjects with erythrocyte glucose-6-phosphate dehydrogenase deficiency had levels of this enzyme in liver tissue of 0·052 and 0·040 units. 6-Phosphogluconic dehydrogenase activity in the liver of these subjects were 0·15 and 0·13 units compared with levels of 0·12, 0·17, 0·13 and 0·20 units in the control subjects, respectively.

These findings are of importance with respect to identification of the primary action of the genetic factor responsible for the deficiency in glucose-6-phosphate dehydrogenase in red cells of 'drug-sensitive' subjects. If the erythrocyte enzyme deficiency resulted from the direct action of a gene locus, all tissues of the affected organism might be expected to exhibit the lowered enzyme activity. The present studies suggest that erythrocyte glucose-6-phosphate dehydrogenase deficiency is not a primary but a more remote consequence of the presence of a genetic defect. No evidence for a glucose-6-phosphate dehydrogenase inhibitor was found in these red cells[9]. There is little or no protein synthesis in the mature erythrocyte[10,11]. As normal red cells age *in vivo*, there is a decrease in glucose-6-phosphate dehydrogenase activity[12]. A deficiency in erythrocyte dehydrogenase might result from an action of the gene affecting the turnover or stability of this enzyme in a manner such that its activity decreases more rapidly than normal as the red cell ages *in vivo*. Studies on the effect of age on glucose-6-phosphate dehydrogenase in erythrocytes of subjects whose red cells are deficient in this enzyme have revealed that young red cells have markedly higher activities than older cells[9].

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Ageing of Human Cartilage

IN a recent study of human costal cartilage, the isolation of kerato-sulphate in addition to chondroitin sulphate was reported in two cases of Marfan's syndrome and in two young adults free of skeletal abnormalities[1]. In earlier work on hyaline mammalian cartilage, including that of new-born infants, no keratosulphate fraction had been encountered[2]. Moreover, rib cartilage of the new-born yielded only chondroitin-4-sulphate (*A*), while in the adult the fraction was predominantly chondroitin-6-sulphate (*C*)[3]. These findings, as well as the demonstration of a shift from D-galactosamine to glucosamine with increasing age in epiphyseal human cartilage[4], suggested a study of the distribution of chondroitin sulphate and keratosulphate in rib cartilage of various age-groups.

Human rib cartilage was obtained at unselected autopsies (we thank the Department of Pathology for its collaboration in this connexion). The age ranged from new-born to 74 years. The ribs were cleaned of extraneous tissues, bony parts and perichondrium, and dried in acetone. The dried tissue was homogenized, digested with 'activated' commercial papain[5] at 70°C. (Scott, J. E., personal communication) and, after further purification, the acid mucopolysaccharides were fractionated and analysed for nitrogen, hexosamine, uronic acid, hexose and sulphate. A quantitative separation of chondroitin sulphate and keratosulphate was not attempted since in our experience separation of keratosulphate from chondroitin-6-sulphate has only been possible after enzymatic digestion of the latter with testicular hyaluronidase. The chondroitin sulphate and keratosulphate content of the fractions were calculated from the carbazole and anthrone values of the isolated fractions.

The chondroitin sulphate of the fractions as per cent dry weight of cartilage is shown in Fig. 1. The chrondroitin sulphate content appears to decrease

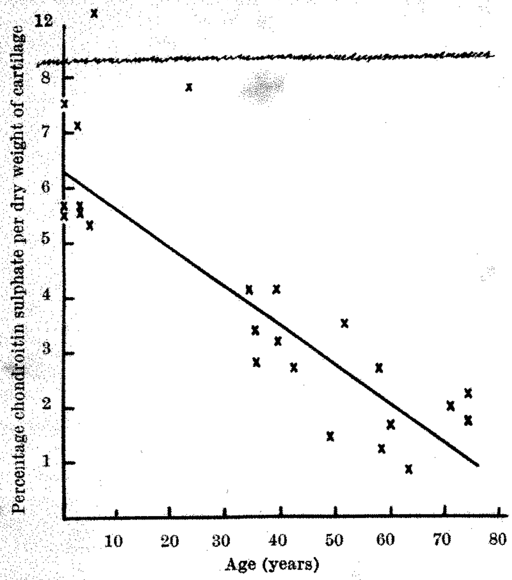

Fig. 1. Chondroitin sulphate content as percentage of dry weight of rib cartilage in relation to age

linearly with age. Keratosulphate was negligible or absent in the very young. It appears to reach a plateau at 20–30 years and to remain constant to the greatest ages investigated, where it represented approximately 50 per cent of the total mucopolysaccharide. When the ratio of keratosulphate to the total mucopolysaccharide is plotted against age, a linear increase is obtained as shown in Fig. 2. In this curve, the two cases of Marfan's syndrome (encircled crosses) fall within the upper range of the normal. Furthermore, costal cartilage from a young cow and a young pig, and tracheal cartilage from a young cow demonstrated similar ratios of keratosulphate to total mucopolysaccharide as do immature human beings.

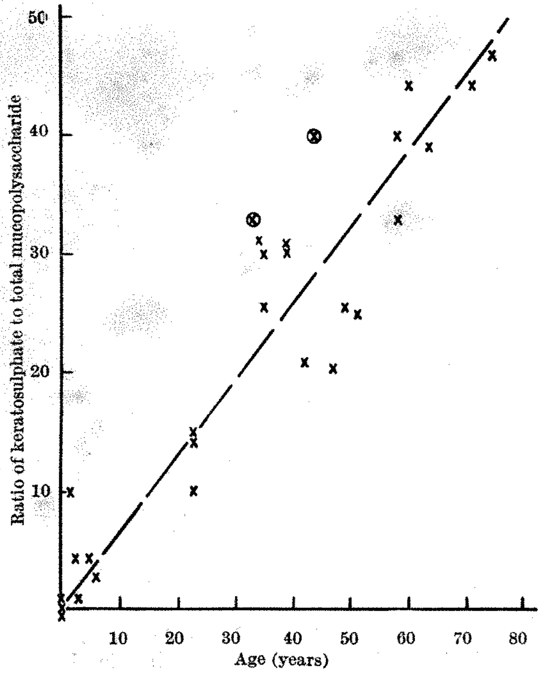

Fig. 2. Ratio of keratosulphate content to total mucopolysaccharide of rib cartilage in relation to age

Clinically, no correlation was found with sex (2/3 male, 1/3 female), with presence and degree of arteriosclerosis, or the state of nutrition (judged by degree of wasting as noted at autopsy). It may also be of interest that two of the subjects were on steroid therapy for more than two years, one had moderate osteoarthritis, one 34-year-old had bone disease and mild diabetes secondary to Cooley's anæmia.

The rib cartilage appears to be a tissue eminently suited for studies on ageing because it is less affected than other tissues by mechanical stresses, by the repeated insults of infection, and by the nutritional status. While the decrease in chondroitin sulphate content is continuous from birth to old age, the keratosulphate content increases to a plateau, which appears to be maintained even in senescence. The process of change with time in cartilage is thus more comparable to differentiation rather than to degeneration usually associated with ageing. It will be of interest to determine whether the time-schedule apparently inherent in this tissue can be influenced experimentally.

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Salt Concentration and Fibrinolytic Activity

THE observation of gross spontaneous lysis in pathological states presents little difficulty, so long as there is some fibrinogen left to form an observable clot; but there is still no satisfactory method of assessing the normal blood fibrinolytic activity. The different test systems all disturb the balance of the fibrinolytic system, for example, by dilution, fractionation or introduction of abnormal clotting systems or change of *p*H. It is still debatable whether any method even approaches the state of affairs in a normal vessel, still less that in a thrombotic case where deposition of fibrin probably leads to local absorption of fibrinolytic components so that active enzyme is produced locally and clot lysis facilitated. This latter aspect is not directly approachable by *in vitro* methods; but it draws its reactants from the circulating blood, though in injury or anoxia tissue factors are also important, and so one aspect of the body's ability to deal with a clot is reflected in the blood fibrinolytic activity.

By apparently minor changes in the experimental conditions enormous variations can be produced in the fibrinolytic activity of the same blood sample. To compare results it is necessary to have a rigidly standardized assay system, and sufficient attention

Table 1. EFFECT OF VARYING SODIUM CHLORIDE CONCENTRATION ON PLASMA FIBRINOLYTIC ACTIVITY BY PARTIAL LYSIS METHOD

Plasma	Sodium chloride in reaction mixture (per cent)	6-hr. lysis	24-hr. lysis
1	0	14·5	100
	0·3	75	100
	0·6	13·5	100
	1·0	0	97
2	0	50	100
	0·25	96	100
	0·5	26	100
	0·75	3	80
	1·0	0	4·5

Table 2. LYSIS TIMES (MIN.) OF BOVINE FIBRINOGEN BY STREPTOKINASE-ACTIVATED HUMAN PLASMA

Sodium chloride in reaction mixture (per cent)	Plasma 1	Plasma 2	Plasma 3
0	49	42	43·5
0·2	17	21	21·5
0·4	14	18	18
0·6	15	17·5	19·5
0·8	18	20	21
1·0	28·5	24	31

has not been paid to the effect of salt concentration. We show here some typical results of varying the salt concentration on the fibrinolytic activity of fresh, cold-collected, citrated human plasma as measured by the partial lysis method (Table 1) and on the total potential fibrinolytic activity as measured by streptokinase activation followed by lysis of bovine fibrin (Table 2).

Further experiments have shown that this effect is also obtained with salts other than sodium chloride, and there appears to be a relationship between fibrinolytic activity and the ionic strength of the reaction mixture. These results will be reported fully elsewhere.

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Characterization of a Second Yellow Compound from *Drosophila melanogaster*

Hadorn and Mitchell[1] demonstrated by simple chromatographic techniques the presence of two yellow, yellow-fluorescent compounds in *Drosophila melanogaster*. Both these compounds are accumulated in the *sepia* mutant, and one of them (*F* 1 5), which is by far the major component, has been isolated in crystalline form[2]. A structure has been postulated for it[3], although this has had to be modified recently in the light of some new experiments on the compound to be described in this communication. The second component (*F* 1 7) is present in extremely small amounts even in the *sepia* mutant, and at such low levels it is very sensitive to light. However, we have succeeded in isolating a small amount of this material in crystalline form and have been able to demonstrate that it is indistinguishable from a yellow compound (compound *A*) which is found in comparatively large quantities in the blue-green alga, *Anacystis nidulans*[4,5].

A 6 per cent trichloracetic acid extract of 30 gm. of flies (*D. melanogaster*; mutant *sepia*) was passed through an acid-washed 'Florisil' column. The yellow fluorescent materials were concentrated in a band at the top of the column, and after the column had been thoroughly washed with dilute acetic acid and water, this band was eluated with 20 per cent aqueous acetone. The eluate was concentrated and then streaked on heavy filter paper (Whatman No. 17). A descending chromatogram was developed with butanol/acetic acid/water (4 : 1 : 1), and the faster-moving yellow compound was collected as a fraction when the solvent was allowed to drip off the paper. After evaporation of this fraction to dryness in the dark and *in vacuo*, a solution of the residue was again passed through a 'Florisil' column. The yellow eluate obtained by washing this with 20 per cent acetone was evaporated to small bulk, when the product crystallized in tiny yellow needles.

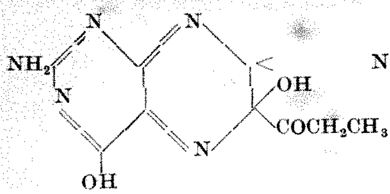
The absorption spectrum of this material was identical with that of the main yellow substance from *Drosophila* and with compound *A* from *Anacystis nidulans*[2,4]. Its paper chromatographic behaviour was identical with that of compound *A* (Table 1). Furthermore, on decomposition with bromine water, a colourless, blue-fluorescent material was obtained which again was identical paper chromatographically and spectroscopically with the analogously prepared derivative of compound *A*. Lastly, in alkaline solution, this yellow compound was readily oxidized to xanthopterin—again[5] a characteristic reaction of compound *A*.

Table 1

Solvent	R_F			
			Bromine decomposition products	
	Compound *A*	*F* 1 7	Compound *A*	*F* 1 7
n-Propanol/1 per cent ammonia (2 : 1)	0·78	0·78	0·82	0·82
n-Butanol/acetic acid/water (4 : 1 : 1)	0·75	0·75	0·73	0·73
n-Butanol/methylethyl ketone/ammonia/water (5 : 3 : 1 : 1)	0·21	0·21	0·23	0·23
sec.-Butanol/formic acid/water (8 : 2 : 5)	0·32	0·32	0·27	0·27

Drosophila melanogaster, then, contains as a normal constituent, albeit in very small amount, the same yellow pteridine as is found in *Anacystis nidulans* and which is probably xanthopterin B_1[6] and bufo-yellow 2[7]. The structure proposed for this compound (I) and the revised structure for the main yellow pigment from *Drosophila* (II), show that they are quite simply related, I being the deoxy derivative of II. It is not difficult to visualize how the two side-chains on these compounds could arise from a common precursor, the dihydroxypropyl side-chain of biopterin (III), by simple dehydration or oxidation. Whether these reactions occur biologically remains to be discovered.

The implications of these findings for the structures of the red eye pigments of *Drosophila* might also be outlined. There are at least three red eye pigments[8]. The presumed precursor for these is the main yellow compound accumulated by the *sepia* mutant which has no red eye pigments. It is possible, however, that the three red compounds arise from three different, but closely related, yellow precursors, two of which are mentioned in this communication, a third remaining to be discovered (a third possible compound, for example, would be one containing a $CH_2OHCHOHCO$— side-chain at the 6-position.



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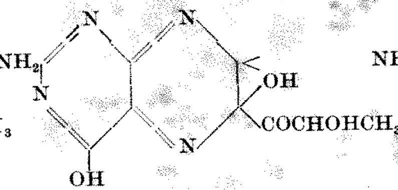

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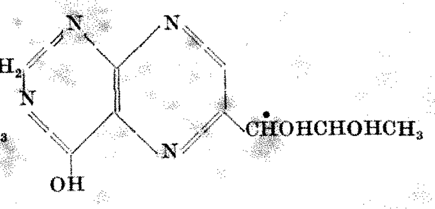

III

This would be reasonable in view of the similar biological activity of biopterin and its trihydroxypropyl analogue[9]). A simple chemical change, for example hydroxylation of the 7-position, or further oxidation would then convert these yellow compounds into the closely related red pigments. Further work on this aspect and on the biochemistry of these compounds is being undertaken.

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Activity of 10-Hydroxydecenoic Acid from Royal Jelly against Experimental Leukæmia and Ascitic Tumours

Despite many investigations of royal jelly[1], its chemistry and pharmacological activity have not been completely established. As part of a long-term study on the chemistry and biological activity of royal jelly[2] we have recently investigated its possible anti-tumour properties. In this communication we wish to report that admixture of royal jelly with tumour cells before inoculation completely suppresses the development of a transplantable mouse leukæmia and the formation of ascitic tumours in mice. Fractionation studies have established that this anti-tumour activity resides in the main fatty acid of the royal jelly—10-hydroxydecenoic acid.

Anti-leukæmia studies were carried out by the method of Burchenal *et al.*[3] using female mice, 5–6 weeks of age, of the *AKR* strain. Cell suspensions were prepared in Gey's balanced salt solution[4] from the spleen of a mouse dying from spontaneous leukæmia. To these suspensions were added whole royal jelly, various fractions of royal jelly, or a standard citric acid or phosphoric acid buffer. The *p*H of each mixture was determined. The mixture was then shaken and immediately injected subcutaneously at a dose of 0·2 ml. per mouse. Each mouse received 2–5 million cells, as measured by direct hæmacytometer counts. Mixing of the tumour cells with test materials prior to injection has been employed in other investigations of a similar nature[5].

The criterion used in these experiments was survival: the mice either developed leukæmia or were protected. Each dead mouse was examined both grossly and microscopically by liver and spleen section to determine the extent of leukæmia infiltration. First transfers from mice with spontaneous leukæmia caused death in approximately 50 days; but successive transfers caused death more rapidly, in some cases within 16 days. The results of the anti-leukæmia experiments are summarized in Table 1.

Table 1. EFFECT OF ROYAL JELLY AND 10-HYDROXYDECENOIC ACID ON SURVIVAL OF MICE WHEN MIXED WITH LEUKÆMIC OR ASCITIC TUMOUR CELLS PRIOR TO INJECTION

Mixture*	No. of mice	*p*H of mixture	Protection†
Leukæmic cells plus:			
30 mgm. fresh royal jelly	41	4·2–4·8	+
15 mgm. fresh royal jelly	14	5·5–6·5	–
1·5 mgm. 10-hydroxydecenoic acid	32	4·2–4·8	+
1·0 mgm. 10-hydroxydecenoic acid	12	5·1–6·1	–
Citric acid buffer only	7	4·2	–
Phosphoric acid buffer only	16	5·3–5·8	–
2·0 mgm. 10-hydroxydecenoic acid	20	4·7–5·6	+
2·0 mgm. 10-hydroxydecenoic acid	26	6·1–7·3	–
6C3HED lymphosarcoma cells plus:			
100 mgm. whole royal jelly	212	5·9–6·1	+
100 mgm. whole royal jelly	52	7·2	–
1·0 mgm. 10-hydroxydecenoic acid	28	4·2	+
1·0 mgm. 10-hydroxydecenoic acid	28	6·9	–
0·6 mgm. 10-hydroxydecenoic acid	24	4·2	–
Buffer only	64	4·2	–
Buffer only	278	6·9–7·4	–

* Materials indicated as mgm. per ml. of cell suspension. In leukæmia experiments, each mouse received 0·2 ml. of mixture; in ascites experiments, each mouse received 0·5 ml. of mixture.

† +, Survival beyond six months. –, 100 per cent death in 21–54 days with the leukæmic cells and 100 per cent death in 12–15 days with *6C3HED* cells.

Anti-tumour studies were conducted in three lines of ascitic tumours: the *6C3HED* lymphosarcoma, the *TA3* mammary carcinoma, and the Ehrlich carcinoma. Initially, these tumours were carried in the tumour-specific mouse strains; but in later experiments all three tumours were carried in the non-specific Connaught mouse line, following the freezing procedure of Morgan *et al.*[6]. Ascitic cells were harvested by intraperitoneal puncture, mixed with 2 vol. water to lyse any red cells present, centrifuged, and resuspended in Hanks's balanced salt solution[7] to the desired cell count. This suspension was mixed with the appropriate amount of whole royal jelly or fraction of royal jelly at different *p*H-levels, and was then administered intraperitoneally to large groups of mice (10–30) in 0·5-ml. doses. Each mouse normally received 5–8 million tumour cells; but in some cases doses of 10–20 million cells were used.

As in the anti-leukæmia experiments, the criterion was survival: control mice died from ascitic tumours in less than 14 days, while mice receiving appropriate mixtures of cells and royal jelly all failed to develop tumours. Protected mice were kept under observation for 90 days after death of the control mice. They were then killed, and random individuals autopsied to confirm the absence of tumours. The results of these studies are also summarized in Table 1. To conserve space, only experiments with the *6C3HED* lymphosarcoma are reported, although identical results were obtained with the other two tumours, and only the active fraction, 10-hydroxydecenoic acid, is listed.

The results summarized in Table 1 indicate that 30 mgm. of fresh whole royal jelly or 1·5 mgm. of 10-hydroxydecenoic acid per ml. of cell suspension inhibited completely the development of transplantable leukæmia in *AKR* mice. This effect was obtained only when the active material was mixed with the leukæmic cells prior to administration. Attempts to demonstrate protection after tumour implantation or by separate administrations of royal jelly and leukæmic cells have as yet been unsuccessful. The anti-leukæmic activity was demonstrated only at *p*H values below 6·0; but leukæmic cells alone, buffered to the same *p*H-range, caused death from leukæmia within the normal time.

Results of the anti-ascites experiments (Table 1) are very similar to the anti-leukæmia observations. Both whole royal jelly and its constituent 10-hydroxydecenoic acid prevent the development of ascitic tumours in mice. Somewhat higher concentrations of material are required than with the transplantable leukæmia. Approximately 100 mgm. of fresh whole royal jelly or 1·0 mgm. of 10-hydroxydecenoic acid per ml. of cell suspension were required for complete protection. At lower dosages, development of the ascitic tumours was delayed for 5 to 6 days. Afterwards, rapid tumour formation and death of the mice ensued in all cases. As in the leukæmia experiments, an acid *p*H and admixture of the royal jelly or fatty acid with the tumour cells prior to injection were required to demonstrate the activity.

The role of royal jelly in the development of queen bees has stimulated many investigations into its possible therapeutic role in many human diseases, including leukæmia[8]. In most instances, the reports have been incomplete and difficult to assess. The present report appears to be the first unequivocal demonstration of an anti-tumour activity in royal jelly. The results have been confirmed repeatedly on nearly 1,000 mice during a 2-year period, and show a striking effect: either all the mice die quickly or all survive. Two groups of mice which received tumour cells plus royal jelly remained alive and healthy more than 12 months after inoculation, while sister mice which received the same number of tumour cells without royal jelly died within 12 days.

The royal jelly ether-soluble fatty acid used in this study was isolated originally by Townsend and Lucas in 1940[2] and was later identified by Butenandt[9] as 10-hydroxydecenoic acid. The dependence of its biological activity on *p*H suggests that only the undissociated fatty acid is effective. Identification of the active constituent of royal jelly as a fatty acid is of interest in view of the recent demonstration[10] that ascitic tumour cells can metabolize such compounds readily.

Further studies are in progress to determine whether the active material causes death of the tumour cells before inoculation, as reported previously by Burchenal *et al.*[11] with certain chemotherapeutic compounds. The study has been extended to an investigation of structural derivatives of 10-hydroxydecenoic acid and closely related compounds.

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Serotonin and Change of Colour in Frogs

It is well known that intermedin, a secretion of the pituitary, is responsible for the dispersion of the pigment in the melanocytes of frogs. The identity of the secretion has remained a mystery; indeed, there are few compounds capable of causing the darkening of hypophysectomized frogs.

Recent experiments in this laboratory have revealed that the indolamines tryptamine and 5-hydroxytryptamine (serotonin) disperse the pigment in the melanocytes of hypophysectomized specimens of *Rana pipiens* when injected into the dorsal lymph space. The effect, recorded by photographing an area of the web of the foot at intervals after the injection, is short-lived; dispersion of the pigment is apparent within 15 min. after injection and lasts an additional 15–30 min. At the end of this time, the pigment returns to its normal concentrated condition, but some reinforcement of the effect can be obtained by a second injection while the pigment is dispersed. The degree of dispersal achieved during these experiments does not approach that encountered in a fully darkened frog in Nature, but the effect is definite and striking. The chemicals were administered as solutions in Ringer's solution of tryptamine hydrochloride and 5-hydroxytryptamine creatinine sulphate in doses ranging from 10 to 1,000 μgm.

Other compounds with pharmacological properties similar to those of serotonin have been tested and found to exert no melanophorotropic effect. Thus, in the present study, histamine acid phosphate and acetylcholine bromide failed to disperse the pigment, and Hogben and Winton[1] found that tyramine was without effect.

Extracts of frog pituitary gland in Ringer's solution produce total dispersion of the pigment lasting several hours when injected into hypophysectomized frogs. Injection of 100 µgm. of lysergic acid diethylamide, considered to be an inhibitor of serotonin, with the pituitary extract results in a return of the pigment to the contracted condition much more quickly. This experiment can be regarded as providing indirect evidence that serotonin is involved in the darkening process. A similar antagonism between serotonin and lysergic acid has already been reported for the chromatophores of fish[2].

Using an extraction technique based on that of Weissbach, Waalkes, and Udenfriend[3], extracts have been prepared from frog pituitary glands. When such extracts are evaporated to dryness to eliminate the toxic organic solvents involved in the extraction process, and the residue is dissolved in Ringer's solution, they exhibit melanophorotropic activity in the same way as the indolamines when injected into hypophysectomized frogs. On the other hand, an extract prepared from frog nerve cord has no effect.

However, ultra-violet absorption studies with these extracts have demonstrated that the material is not serotonin. The hypothesis that it may be a derivative or precursor of 5-hydroxytryptamine is under examination in this laboratory.

I am indebted to Dr. W. E. Beckel, in whose laboratory this work is being done, for his interest and encouragement, and to the National Research Council for financial support.

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Lack of Effect of Histidine on Rabbit Atheromatosis

CHIMAKADZE[1,2] has published an interesting report on the treatment with histidine of rabbits fed with cholesterol. He claimed that daily administration of 80 mgm. of histidine for 20 days lowered the serum cholesterol-levels by 1,000–1,300 mgm. per cent and markedly diminished the deposition of aortic lipids. In view of the potential importance of these claims we decided to repeat and extend the experiment.

Twenty-one white New Zealand rabbits from four litters (litters I, II, III contained 5 animals, litter IV, 6 animals) were divided into five groups. Each group was composed of one member from each litter; the fifth group had 2 litter mates. Groups 1 and 2 were given 100 gm. 'Purina' rabbit chow containing 0·375 gm. cholesterol a day. Groups 3 and 4 received the same amount of chow containing 0·750 gm. cholesterol a day. Group 5 served as a control to check possible hereditary hypercholesterolæmia or the presence of spontaneous aortic lesions. The animals received the diets for 92 days, and food consumption records were obtained for each animal. After the first 50 days the rabbits of groups 1 and 3 were given by stomach tube 80 mgm. of histidine in 4 ml. water a day. (DL-Histidine hydrochloride was chosen since Chimakadze did not specify the type of histidine used, and since experiments in rats[4] and mice[5] have shown that D-histidine is converted to L-histidine.) The animals of groups 2 and 4 were given by stomach tube 4 ml. of water only. Serum cholesterol was determined by the method of Pearson *et al.*[3] before starting the cholesterol diet, every 10 days during the first 50 days, and once each week during the remainder of the period. The evaluation of the degree of the aortic lipid deposition was made by gross observations of the excised aortas according to a standard scale employed in our laboratory.

Animals fed with the lower cholesterol diet showed the same degree of slight atheromatosis, those fed with the higher cholesterol diet the same degree of more severe lesions into the aortic wall. Thus our results have shown no difference in the extent of lipid deposition in the aortic wall of the histidine-treated group when compared with the animals receiving water. The serum cholesterol-levels showed a gradual increase from the initial levels of 117 ± 9 mgm. per cent to final levels of 363 ± 171 mgm. per cent on the 0·375 gm. cholesterol intake and 1,073 ± 115 mgm. per cent on the 0·75 gm. cholesterol intake on the fiftieth day.

During the 22 days of histidine administration, when Chimakadze claimed a decrease of serum cholesterol by 50 per cent, 5 out of 7 of our water-treated group and 5 out of 6 of our histidine-treated group showed further and similar increases in their serum cholesterol-levels. We did not note any differences in cholesterol-levels in the different groups up to 37 days of histidine treatment, which was nearly twice as long a time as that employed by Chimakadze. At that time some of the histidine-supplemented animals developed some anorexia and the experiment was terminated. The animals in the control group were free from an elevation of the blood cholesterol-level or aortic fat deposits.

On the basis of our results we cannot explain the pronounced effect of histidine claimed by Chimakadze. The administration of 80 mgm. of histidine does not increase the total histidine intake significantly, since the animals already received 430 mgm. of histidine daily ('Purina' rabbit chow contains 0·43 per cent L-histidine; personal communication from P. E. Kifer, Ralston Purina Company.) Perhaps the Russian diets, which are not specified by the author, were marginal in histidine content. It is also possible that in the Russian experiment the administration of histidine altered the food intake, a factor which was controlled in our experiment but not mentioned by Chimakadze. A third possible difference may, of course, be in the strain of the animals.

In conclusion, it is apparent that the alleged lowering of cholesterol and anti-atherogenic activity of histidine could not be demonstrated under the conditions of our experiment.

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Reserpine Derivatives with Specific Hypotensive or Sedative Activity

RECENTLY it has been reported, by Ciba Laboratories[1,2], that two reserpine analogues show more specific effects than reserpine. Methyl-18-O(3-NN-dimethylaminobenzoyl)reserpate (or *SU* 5171) exhibits sedative activity, while carbethoxysyringoylmethylreserpate (syrosingopine or *SU* 3118) is effective in decreasing blood tension (see formulæ).

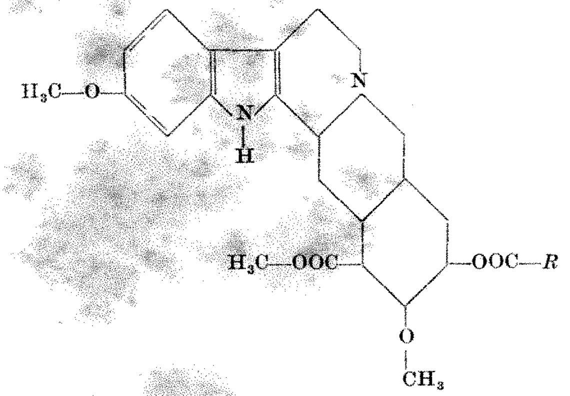
These results prompted us to investigate, on a quantitative basis, the difference between the two new compounds and reserpine during several tests.

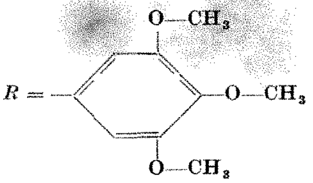
Our experiments were carried out on Sprague–Dawley rats of both sexes, weighing about 200 gm. The compounds were injected intraperitoneally 4 hr. before the determinations reported here were made. Brain serotonin was assayed according to Bogdanski *et al.*[3] by the spectrofluorimetrical method. Blood pressure was recorded kymographically, by a Sanborn electro-manometer, following cannulation of the carotid artery, the animal being narcotized with ethyl urethane (100 mgm./100 gm. intraperitoneally). Body temperature was measured with an electrical thermometer introduced in the rectal cavity. Sleeping time after barbiturates was evaluated by injecting intraperitoneally 20 mgm./kgm. nembutal. Sedation was judged by observation of behaviour, responsiveness to commands and reduced interest in surroundings.

The results obtained are summarized in Table 1.

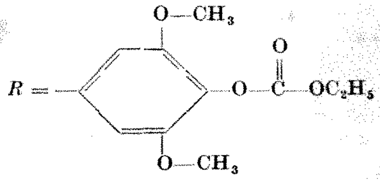
From these results it appears quite evident that *SU* 3118 and *SU* 5171 have, at least in rats, a specific effect. In fact, while for reserpine the minimal hypotensive dose and the minimal sedative dose are very close, for *SU* 3118 and *SU* 5171 they are clearly differentiated. In particular, for *SU* 3118 the onset of sedation occurs at 30 mgm./kgm., while the fall of blood pressure begins at 0·95 mgm./kgm.; for *SU* 5171 the two activities are present respectively at 5 mgm./kgm. and more than 30 mgm./kgm., the highest dose tested. Further experiments indicate that the sedative activity of *SU* 5171 (7·5 mgm./kgm.) is less persistent than the respective activity of reserpine (2·5 mgm./kgm.), since it disappeared after 36 hr.

In agreement with a previous paper of ours on reserpine[4], for these new compounds also good correlation is shown between sedation, depletion of brain serotonin, fall in rectal temperature and increase in nembutal sleeping time. In particular the





Reserpine



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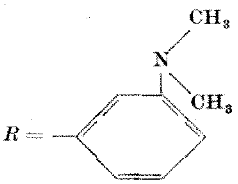

SU 5171

Table 1

Compound	Mgm./kgm. (i.p.)	Blood pressure (mm. mercury) max.	min.	Brain serotonin (gamma/gm.)	Rectal temperature (° C.)	Duration of narcosis after nembutal (min.)	Sedation
Solvent	—	146 ± 7 (40)	83 ± 4 (40)	0·47 ± 0·008 (50)	37·5 ± 0·08 (30)	28 ± 3 (50)	—
Reserpine	0·31	131 ± 7 (10)	51 ± 7 (10)				—
	0·62	125 ± 11 (10)	43 ± 5 (10)	0·42 ± 0·04 (10)			—
	0·95	122 ± 5 (10)	44 ± 7 (10)	0·33 ± 0·02 (10)			±
	1·25	97 ± 4 (10)	55 ± 5 (10)	0·27 ± 0·01 (10)	35·3 ± 0·3 (10)	39 ± 5 (10)	+
	2·50			0·17 ± 0·005 (10)	34·0 ± 0·25 (10)	58 ± 7 (10)	+
	5·00			0·12 ± 0·018 (10)	32·3 ± 0·19 (10)	81 ± 4 (10)	+
SU 3118	0·62	136 ± 3 (10)	64 ± 4 (10)				—
	0·95	119 ± 5 (10)	41 ± 5 (10)				—
	1·25	105 ± 2 (10)	46 ± 2 (10)				—
	2·50	106 ± 3 (10)	50 ± 3 (10)	0·48 ± 0·06 (8)	37·0 ± 0·11 (10)	24 ± 8 (10)	—
	20			0·46 ± 0·005 (8)	36·7 ± 0·17 (10)	35 ± 4 (10)	—
	40			0·20 ± 0·009 (8)	33·2 ± 0·40 (10)	125 ± 7 (10)	±
	50			0·13 ± 0·012 (8)	33·0 ± 0·19 (10)	150 ± 2 (10)	+
SU 5171	2·5			0·48 ± 0·023 (8)	35·2 ± 0·21 (10)	52 ± 2 (10)	
	5			0·25 ± 0·009 (8)	34·7 ± 0·05 (10)	60 ± 1 (10)	±
	7·5			0·12 ± 0·005 (8)	33·6 ± 0·45 (10)	92 ± 2 (10)	+
	10	139 ± 3 (10)	60 ± 10 (10)	0·14 ± 0·012 (8)	33·3 ± 0·18 (10)	119 ± 2 (10)	+
	20	138 ± 5 (10)	70 ± 7 (10)				+
	30	140 ± 6 (10)	55 ± 2 (10)				+

The number of animals used is given in brackets.

release of brain serotonin, induced only by the compound provided with sedative activity, supports Brodie's assumption[5] on the importance of depletion of brain amines in explaining reserpine sedation. On the contrary, the decrease in brain serotonin does not seem significant in explaining the hypotensive effect of reserpine. The possibility that *SU* 3118 is ineffective on brain serotonin for a poor penetration into the brain is questionable, since in some experiments we observed no changes in intestinal serotonin after 20 mgm./kgm., while reserpine (2·5 mgm./kgm.) or *SU* 5171 (7·5 mgm./kgm.) determined a depletion of about 40 per cent. The use of these new compounds, besides their clinical importance[6], seems to be very valuable for a better understanding of the mechanism of the action of reserpine in determining both hypotension or sedation.

For this research we gratefully acknowledge the gift of *SU* 3118 and *SU* 5171 from Dr. A. J. Plummer, of Ciba Laboratories, Summit (N.J.), and of reserpine from Dr. V. Ghetti, of Ciba s.p.A., Milan.

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Differences in Mechanism in Staining Reactions for Mast Cells

Mast cells are usually identified histochemically by the use of aldehyde fuchsin[1], Hale[2] or Rinehart[3] stain, or by the metachromasia they exhibit with certain basic dyes. All these methods demonstrate mucopolysaccharides, although differences in the degree of staining of various mucopolysaccharides with the several methods have been noted[4]. Peracetic acid oxidation (Greenspan's mixture 30 min., 25° C.)[5] of tissue sections has been found to induce staining of certain normally unreactive substances with aldehyde fuchsin[6–8], and to alter the susceptibility of oxytalan fibres to hyaluronidase, lysozyme and elastase[7]. During the course of investigations of mucopolysaccharide reactivity after peracetic acid oxidation, an interesting change was observed in mast-cell cytoplasms. Peracetic acid oxidation followed by digestion with enzymes which hydrolyse mucopolysaccharides resulted in diverse staining reactions with the above three methods for mucopolysaccharides.

The skin, tongue and other organs of adult *BALB/c* strain mice were used. Fresh 2-mm. thick specimens were taken and immediately placed in Lillie's[5] aqueous neutral calcium acetate formalin for 24 hr. at room temperature. The specimens were then washed, dehydrated, blocked in paraffin, and sectioned at 6μ.

Mast cells in control sections stained with either azure *A* (0·5 per cent in aqueous 0·2 *M* phosphate buffer *p*H 4, 30 min., 25° C.), aldehyde fuchsin or the Hale stain reacted brilliantly either with or without previous oxidation of tissue sections with peracetic acid. Peracetic acid generally enhanced the subsequent staining reactions. However, if sections were oxidized with peracetic acid and then digested with either β-glucuronidase (Nutritional Biochemicals Corp., 15 mgm. : 50 ml. 0·1 *M* acetate buffer *p*H 4·5, 24–48 hr., 37° C.) or lysozyme (Worthington, 5 mgm. : 30 ml. 0·2 *M* phosphate buffer *p*H 5·3 24–48 hr., 37° C.), no mast cells were affected by the Hale stain, and few with aldehyde fuchsin. The few that reacted with aldehyde fuchsin were only slightly stained. Nevertheless, all mast-cell granules and their cytoplasms remained strongly reactive with azure *A*; the staining reaction was only slightly reduced, if at all. Occasionally, testicular hyaluronidase (Nutritional Biochemicals Corp., 25 mgm. : 50 ml. 0·2 *M* phosphate buffer *p*H 6, 24–48 hr., 37° C.) would prevent the subsequent Hale staining reaction, but the results were erratic. No effect on any staining reaction was observed if sections were not oxidized with peracetic acid prior to the digestion step. Sections oxidized with peracetic acid and then incubated in the various buffer solutions for the same time-intervals stained with undiminished or nearly undiminished intensity. When peracetic acid-oxidized sections were incubated in either lysozyme or glucuronidase that had been boiled in its respective buffer for 5 min., the same results were achieved as with unboiled enzymes. This is consistent with a previous report that lysozyme retains full enzymatic activity after boiling in acid solution[9]. The effect of boiling on the enzymatic activity of glucuronidase has not been reported. Lysozyme was inactivated by boiling in alkaline buffer at *p*H 9 for 30 min. (confirming a previous report[9]), and mast cells reacted strongly with all stains after incubation in the usual manner with lysozyme treated in this fashion. Meyer *et al.* have reported the inhibition of lysozyme by iodine and hydrogen peroxide[9]. Lysozyme was almost completely inhibited by iodine (Lugol's 1 : 300 buffer), and moderately inhibited by hydrogen peroxide 30 per cent (1 : 15 buffer) as indicated by the nearly normal, and slightly diminished aldehyde fuchsin and Hale staining respectively of mast cells when incubated with lysozyme and inhibitor. Saccharic acid has been reported to inhibit glucuronidase[10]. Mast cells stained moderately with aldehyde fuchsin and the Hale method after incubation in glucuronidase with saccharic acid at 0·01 *M* concentration, but full staining was not achieved even after incubation with glucuronidase in saccharic acid at 0·1 *M* concentration, indicating moderate but not complete inhibition.

These results are compatible with the view that after peracetic acid oxidation, both glucuronidase and lysozyme enzymatically remove a component from mast cells that is stained with aldehyde fuchsin and the Hale stain, and that there remains a component inducing strong metachromasia with azure *A*. Since inhibitors which are not otherwise likely to alter the enzyme prevent the effect on the staining reactions, it is unlikely that the lack of staining with aldehyde fuchsin and the Hale stain in this case represents an uptake of basic protein by acid mucopolysaccharides rendering these groups unavailable to the stains. This type of blockage has been previously reported[11–13]. The reactions clearly demonstrate that although all the above three methods stain mucopolysaccharides, the granules and other cytoplasmic components of mast cells, the staining reactions are not equivalent and probably are not staining the same substance.

I wish to acknowledge especially the technical assistance of Mr. Clifton Link, jun.

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PATHOLOGY

Purification of the Mouse Mammary Carcinoma Agent by means of a Fluorocarbon

THE use of fluorocarbons for removing host cell components from aqueous suspensions leaving viral particles in relatively pure form in the aqueous phase was suggested by Gessler, Bender and Parkinson[1]. Epstein[2] has demonstrated the utility of this technique in the purification of vaccinia and the Rous sarcoma viruses.

Recently we have reported the identification of the mouse mammary carcinoma agent by correlation of its physical and biological properties making use of filtration through 'Gradacol' membranes, ionizing irradiation and free diffusion[3]. In addition, the structural development of the agent *in vitro* in tumour explants has been traced[4]. Since the fine structure of the agent is now believed to be established, it has become feasible to follow purification procedures by electron microscopic examination of thin sections of ultracentrifugalized pellets.

In a typical example, a spontaneous mammary carcinoma weighing 5·5 gm. from a mouse of the *R*III strain was minced and then homogenized in 40 ml. of a solution 0·15 *M* with respect to sodium chloride, 0·02 *M* with respect to sodium phosphate and 0·2 *M* with respect to sucrose (*p*H 7·4) and 20 ml. of 'Freon 113' or 'Genetron 226' ($CF_2Cl\text{-}CCl_2F$) (density 1·6). The homogenization was accomplished with a 'VirTis' homogenizer (The VirTis Co., Gardiner, N.Y.) run at 45,000 r.p.m. for 2 min. The whole fractionation process was carried out in the cold (0–5° C.). The homogenate was then centrifuged at about 300*g* for 1 min., which caused the emulsified 'Freon' to settle out as a gelatinous layer. The aqueous layer containing the virus was removed from above, mixed with half its volume of 'Freon', again emulsified with the 'VirTis' homogenizer for 2 min. and centrifuged at 300*g* for 1 min. The process was repeated five or six times until the supernatant aqueous layer became almost water-clear. As the soluble proteins and lipids are removed by the 'Freon', the amount of 'Freon' which may be emulsified becomes reduced and the excess will remain as clear liquid underneath.

After the last low-speed centrifugation, the supernatant fluid was spun at 3,000*g* for 20 min., and relatively large gelatinous pellets, presumed to be made up of 'Freon' micelles, were formed. The supernatant was then water-clear and contained the

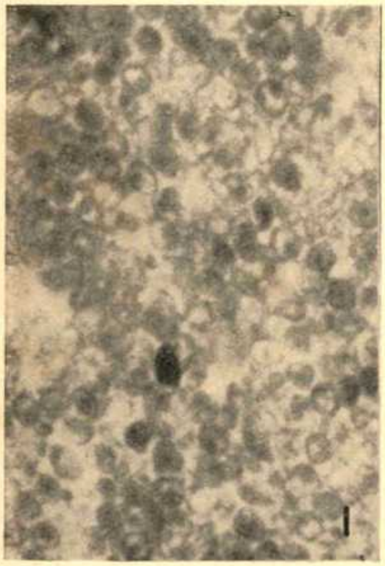
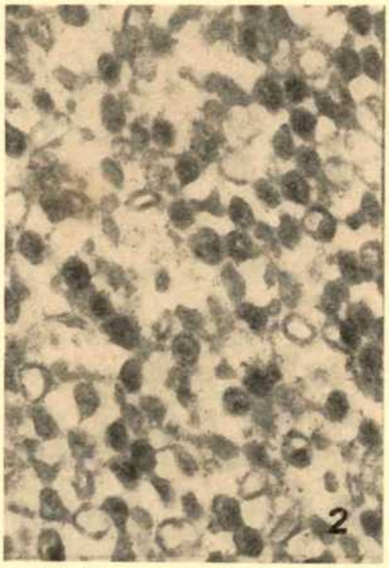
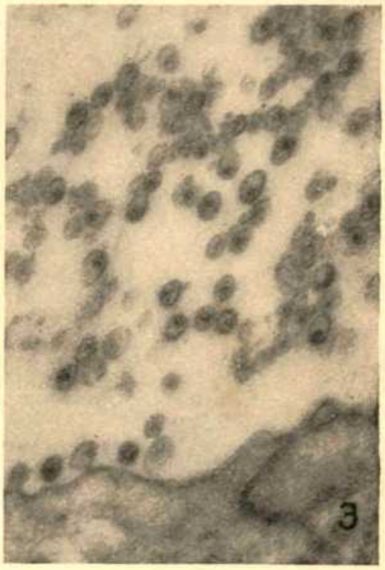

Fig. 1. Electron micrograph of sectioned pellet showing profiles of the milk agent. Since the thickness of the section is less than a third of the diameter of the particles, only segments of many spheres are caught in the section. (× 40,000)

Fig. 2. Electron micrograph of a section from another preparation where the bodies are not so closely packed and the contrast is better. (× 48,000)

Fig. 3. Electron micrograph of mammary carcinoma tissue showing the milk agent particles along the cellular membranes and lying free in the intercellular space. (× 35,000)

desired bodies, which were pelleted out at 100,000g in 1 hr. This small pellet was very white, but turned brown when fixed with 1 per cent buffered osmium tetroxide solution. The pellets obtained after centrifuging at 3,000g did not, on the other hand, turn brown in osmium tetroxide. The fixed pellets were prepared for electron microscopy in the usual manner employed for tissue. Electron micrographs of thin sections of final pellets are illustrated in Figs. 1 and 2. For comparison, Fig. 3 shows the appearance of particles in tumour cells recently identified as the milk agent[3,4].

We have used the same process for purifying the agent from the culture medium of explants of tumour fragments from the *R*III mice, as well as from the milk of these mice. The preparation from the milk was not so pure as those from either the tumours or the culture mediums. Milk is rich in non-viral particles, which are not easily separated by the procedure described here.

Profiles of the milk agent are easily recognizable in the electron micrographs. The characteristic structure of these particles consists of a dense nucleoid about 25 mμ in diameter contained within a membraneous sac about 100 mμ in diameter. The nucleoid occasionally appears centred, but more often it is eccentric, appearing near or in contact with the surrounding membrane. The membrane is 8–10 mμ thick and appears to be of the same structure and density as the membrane of the cells which liberate the bodies[3,4].

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Impairment of Viral Hæmagglutination of Red Cells after Treatment with Formalin

IT was reported recently[1] that mouse cells treated with formalin were more readily agglutinated by some strains of myxoviruses than were untreated cells, and it was suggested that this finding might have general application.

We wish to report briefly that with some viruses and human red cells, the opposite holds good, and that agglutination may be abolished by formalin treatment.

Group O red cells were treated with formalin as described by Gold, Lockyer and Tovey[2]. They were incubated at 37° overnight, then washed three times in saline. Phosphate-buffered saline, pH 7·4, was used as a diluent in the hæmagglutination tests which were carried out in plastic plates at room temperature.

This experiment has now been repeated using the 6-hr. formalin treatment described by Fauconnier and Barua[1], but with phosphate-buffered saline instead of isotonic saline for suspending the cells and for the dilutions. The results were similar to the previous experiment and are given in Table 1.

Table 1. EFFECT OF TREATMENT WITH FORMALIN ON AGGLUTINABILITY OF RED CELLS

Virus strains	Reciprocal hæmagglutination titre		Ratio A/B
	Fresh cells (A)	Treated with formalin for 6 hr. (B)	
Myxoviruses			
Influenza *A* (Mel)	80	80	1
Influenza *B* (Lee)	40	30	1·3
Sendai	8	32	0·25
Columbia *SK**	20	20	1
Adenovirus type 9	6,400	300	21
ECHO viruses			
Type 10	96	< 1	>96
Type 11 (*U* virus[3])	512	<1	>512

* Sheep cells in veronal buffered saline used (ref. 4)

It will be seen that, with the myxoviruses and *Col SK* virus, the titres are either unchanged or enhanced, but that agglutination has been greatly reduced or abolished in the case of the adenovirus 9 and the two *ECHO* viruses tested. Other experiments showed that red cells treated with formalin failed to absorb *ECHO* 10 and 11 viruses, and absorbed adenovirus type 9 less well than untreated cells. Myxoviruses were absorbed equally well by treated and untreated cells. These findings support the view that myxoviruses and *Col SK* virus[4] react with similar red-cell receptors, and that these are distinct from those with which *ECHO* viruses[5] and adenoviruses react.

These results were obtained in the course of an investigation comparing the hæmagglutination reaction found in viruses of various groups and will be published in full later.

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Ploidy of Primary and Metastatic Human Tumours

REPEATED observations conducted over many transplant generations on animal tumours have shown that the modal chromosome ploidy may change during the passages. This change is always toward the higher value of ploidy; changes in the opposite direction have never been observed[1].

Nothing is known about these events in the human tumours since transplantation of tumours from one human being to another is, of course, not feasible. Metastasis in human tumours, however, may be considered a type of self-autotransplantation. The objective of the present study was to compare the cell population ploidy of human primary tumours with that of their metastases. The evidence to be presented was collected from human tumours obtained at surgery (4 breast adenocarcinoma with axillary lymph node metastasis) and at necropsy (1 breast adenocarcinoma with liver and bone metastasis; 1 nasopharyngeal carcinoma with liver and adrenal metastasis).

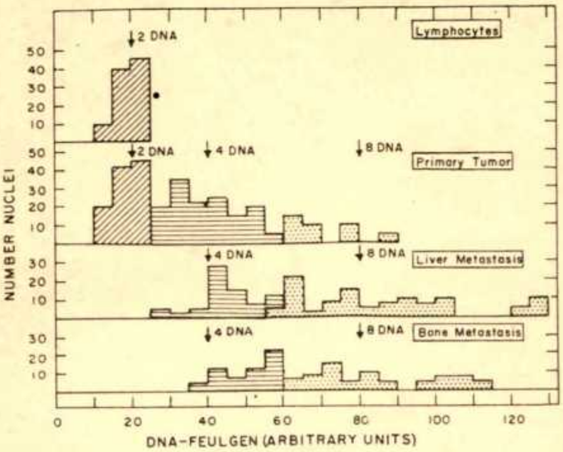

Fig. 1. Distribution in the single nuclei of the deoxyribonucleic acid–Feulgen material in one case of adenocarcinoma of the breast. The arrows correspond to the average value of the single modal class—2 DNA, 4 DNA, 8 DNA are the di-tetra-octoploid classes

With the microspectrophotometric technique, repeated absorption measurements of the deoxyribonucleic acid of single interphase nuclei were made at 546 mμ on Feulgen-stained sections. The product of extinction and volume was taken to be proportional to the amount of deoxyribonucleic acid per nucleus. The total number of nuclei measured for each primary tumour and its metastasis was approximately 500. The primary tumour, its metastasis, and the control lymph node were fixed together, embedded in the same paraffin block and prepared on the same slide. The positive correlation of the quantitative measurement of the deoxyribonucleic acid–Feulgen by microspectrophotometry with deoxyribonucleic acid measurement by ultra-violet microspectrophotometry, with biochemical analysis, and with chromosome counts have established the technique as a suitable method for the evaluation of the nuclear chromosomic set[2,3].

The distribution of deoxyribonucleic acid in the population of cell nuclei of a breast adenocarcinoma is shown in Fig. 1. The histogram shows a first modal class at the same position (2 DNA) for the control lymphocytes and primary tumour cell nuclei. This group of elements corresponds to the diploid class. The 4 DNA and 8 DNA class in the primary tumour nuclei population is an expression of the well-known hetero-polyploid chromosomic condition. The metastatic lesions, localized in the liver and bone (skull) are deficient in the diploid class in comparison with the primary tumour of origin.

The same behaviour was observed in four other cases when the metastatic growth in the lymph node was compared with the primary mammary adenocarcinoma. A similar lack of the diploid class was evident in the liver and adrenal metastasis of a nasopharyngeal carcinoma in contrast to the primary tumour where the diploid class is present. No significant differences were seen between the ploidy of the metastatic lesions in different organs of the same subject. The nuclear volumes of tumour cells were significantly greater in the metastatic lesions and the distribution of the volume estimations had a wider spread than the values found in the primary tumour.

It has been reported that nearly all tumour cell emboli are arrested in the vascular network of the first organ encountered, and that there the earliest and most numerous metastases develop. The concept that these arrested cells always lead to metastatic growth is not in accord with some experimental data from mouse and rat[4–7], with observations obtained from studies in human beings of cancer cells in the blood stream without recognizable metastases (Potter, J. F., and Malmgren, R. A., personal communication) and with the fact that the majority of the arrested emboli apparently fail to produce metastatic foci by extension and growth within the tissues[8–10]. This means that the number of fully established metastatic foci is much less than the number of tumour cells which enters the blood stream and has the opportunity of implantation in a given organ of a subject carrying a malignant tumour.

In the present study the infrequency of diploid cells in the metastasis, in comparison with the primary tumour, suggests the possibility of a cytogenetic basis for the phenomenon of metastasis. It is possible that all types of cells may be released from the tumour and circulate in the vascular or lymphatic stream, but when they become lodged only a few (the hetero-aneuploid) can develop and become established as metastatic loci. Another possible interpretation of the results is that only the heteroploid cells leave the tumour, embolize in the blood stream and establish secondary growths. Whatever the cause, the end-result is a cell population, in the metastasis, differing from the population in the primary tumour. This difference suggests that cells with a heteroploid chromosomic number have a greater capacity for survival and the establishment of metastatic foci when they are transferred to a new site and a new environment.

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BIOLOGY

Infectious Ribonucleic Acid as Precursor of Tobacco Mosaic Virus

In an earlier communication[1], it was reported that the latent period after infection with virus ribonucleic acid is about 10 hr. shorter than after infection with complete tobacco mosaic virus. The simplest explanation for this effect is that the release of ribonucleic acid from the virus takes some time. But even after infection with pure ribonucleic acid, there is a latent period of about 10–20 hr. We have now studied the events during this remaining period in some detail. It seems possible that the first event after infection is a multiplication of the released ribonucleic acid and that a certain amount of it has to be formed before the synthesis of the virus protein can be initiated ; this protein will later combine with the ribonucleic acid to form the complete virus.

Infectious ribonucleic acid cannot be detected when the extraction is carried out with aqueous solutions because it is destroyed by the ribonuclease present in the tobacco leaves. To determine the free ribonucleic acid in the presence of virus nucleoprotein we used the following technique. Leaves of infected *Nicotiana tabacum* (Samsun) were homogenized in the presence of phenol and phosphate buffer. Thus the enzymes of the leaves are destroyed immediately after disruption of the cells and the infectivity of the ribonucleic acid is preserved and can be determined after removal of the phenol phase. By this extraction we obtain the total ribonucleic acid (that is, free ribonucleic acid plus virus-ribonucleic acid). In parallel experiments the amount of virus or virus-ribonucleic acid was determined by two different methods. Part of the same tissue was extracted by buffer without phenol, and the amount of complete virus was bio-assayed on *N. glutinosa* as already described[1]. Since tobacco mosaic virus produces many more local lesions than virus-ribonucleic acid, the ratio of free ribonucleic acid to virus-ribonucleic acid can be calculated only indirectly by this method. To determine directly the ribonucleic acid bound in the virus the infected leaves were homogenized with buffer as before and the solution was incubated for 1 hr. at 37° C. to inactivate the free infectious ribonucleic acid. Ribonucleic acid which is within the virus remains intact after this treatment. The protein was then extracted with phenol and the activity of the liberated virus-ribonucleic acid was measured.

Several series of experiments were carried out in the following way. Young plants of *N. tabacum* (Samsun) were infected with a solution of 10^{-6} gm. tobacco mosaic virus per ml. as previously described[1]. The plants were kept under constant illumination at 23° C. After certain intervals the primarily inoculated leaves were harvested. For each determination eight plants were used. Part of these leaves was homogenized with 0·01 *M* phosphate buffer at *p*H 7·2 and phenol. The phenol was removed with ether and the aqueous ribonucleic acid solution was used for the local-lesion test. The remaining leaves were homogenized with buffer alone. An aliquot of this latter extract was used for the determination of the complete virus. The main portion was incubated at 37° and treated with phenol afterwards for the determination of the virus-ribonucleic acid.

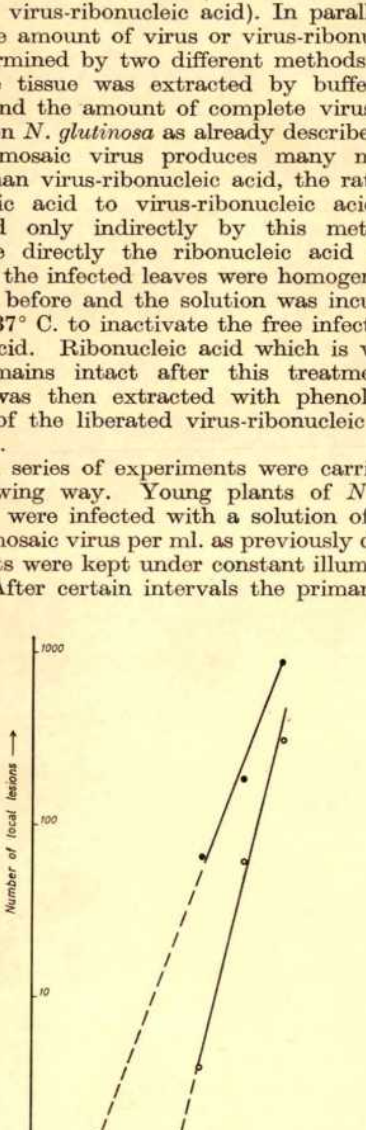

Fig. 1. Increase of total infectious ribonucleic acid, ●——●, and complete virus, ○——○, in *Nicotiana tabacum* measured by the local-lesion test on *Nicotiana glutinosa*

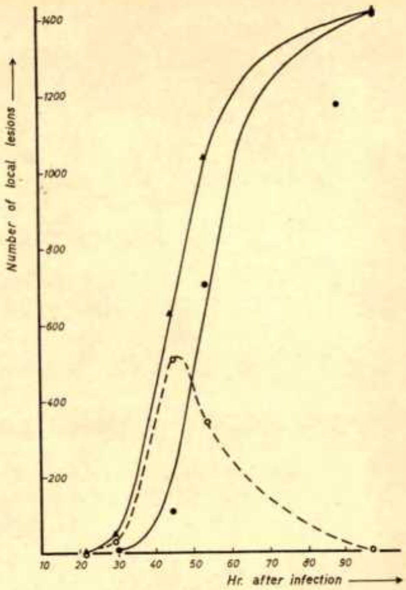

Fig. 2. Increase of total infectious ribonucleic acid, ▲——▲, virus-ribonucleic acid, ●——●, and free ribonucleic acid, ○- - -○, in *Nicotiana tabacum* after infection with tobacco mosaic virus measured by local-lesion test in *Nicotiana glutinosa*

Results of two typical experiments are illustrated in Figs. 1 and 2. In Fig. 1 the increase of total infectious ribonucleic acid and of complete virus measured by the number of local lesions is plotted on a logarithmic scale. At first the activity of the total infectious ribonucleic acid was much greater than the activity of the complete virus. 18 hr. after infection, the total ribonucleic acid produced 68 lesions and the virus only 4. As tobacco mosaic virus produces per mole about 1,000 times as many local lesions as ribonucleic acid, the amount of free ribonucleic acid is about 17,000 times that of the tobacco mosaic virus ; 22 hr. after infection the ratio was about 4,000. In Fig. 2 the numbers of local lesions produced by the total ribonucleic acid and by the virus-ribonucleic acid obtained after incubation and phenol treatment are compared. The difference between the two curves (representing the free ribonucleic acid) is also plotted. It is interesting that the amount of free ribonucleic acid reached a maximum after about 45 hr. and decreased to a small value after 100 hr.

The experiments show that, after infection, a considerable amount of infectious ribonucleic acid is produced before the synthesis of the virus protein starts. This infectious ribonucleic acid, which is not incorporated in the virus, is called free ribonucleic acid. Of course, it is not certain whether it is really free or bound to some other unknown material. From Fig. 2 it can be seen that the difference of time between the rise in free ribonucleic acid and the incorporation of ribonucleic acid in the virus is about 10 hr. For the envelopment of one molecule of ribonucleic acid more than 2,000 peptide sub-units are necessary. An estimation of the rate of production of ribonucleic acid and virus leads to the conclusion that protein is produced more rapidly than ribonucleic acid. Thus, the amount of free ribonucleic acid is reduced by combination with this protein.

In earlier experiments it was demonstrated that during the latent period complete virus is not detectable. Our results give a plausible explanation of this fact. After the entrance of the virus into the cell, the virus particles disintegrate to form ribonucleic acid and protein. The ribonucleic acid multiplies first. The synthesis of the protein starts several hours later, but is much faster. Therefore the amount of free ribonucleic acid reaches a maximum, and decreases afterwards as a consequence of combining with the protein. The latent period in the multiplication of the virus is mainly due to the fact that the release of the ribonucleic acid and its multiplication take some time before the formation of the protein and of the complete virus starts.

Further evidence of free ribonucleic acid as a precursor of tobacco mosaic virus is the inhibition of virus multiplication when ribonuclease is introduced before, or shortly after, the virus[2,3]. The presence of infectious ribonucleic acid in tobacco plants infected with tobacco mosaic virus was also deduced by Cochran[4] from chromatographical experiments.

We are grateful to the Deutsche Forschungsgemeinschaft for financial support.

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A New Method for the Microbiological Oxidation of Steroids

The microbiological steroid transformations in the preparation of sex- and adrenocortical hormones opened a new field for the use of micro-organisms in organic synthesis. An interesting feature of these reactions is the ability to transform substances which are practically insoluble in water in an aqueous medium. It seems obvious that this transformation does not take place in the aqueous phase itself but on the lipoid surface of the micro-organisms. When the fermentation broth and the mycelial mass are treated separately after such transformations, the fermentation broth contains relatively more polar transformation product and less starting material, whereas considerable quantities of the initial steroids could be recovered from the mycelial mass.

Peterson and Murray[1] reported an 80–90 per cent yield of 11α-oxyprogesterone, prepared with *Rhizopus nigricans* from progesterone, and they also found 6β-11α-dioxyprogesterone and 11α-oxyallopregnanedione in the broth. Our strain of *Rhizopus nigricans* gave a 60–70 per cent yield with the dioxy-compound as a by-product. In a fermentor, using glucose, corn-steep liquor, and sodium chloride for the culture medium, and about 10^8 spores per litre for the inoculation, *R. nigricans* grows as a voluminous mucous mass. If the inoculum consists of 10^5 spores per litre it grows in pellets, that is, globules 3–4 mm. in diameter. In our experiments, 400 ml. from a culture of this type were placed in a chromatographic column of 4 cm. diameter fitted with a sintered glass plate, No. *G*–1. The apparatus is shown in Fig. 1. The fluid rises through the lower four-way joint (1) into the glass tube (2), placed alongside the column, the bent part of which reaches into the column. Air is blown through a capillary (3) and thus the broth is continuously forced from the tube into the column and saturated with air at the same time. To the fluid thus kept in constant circulation 160 mgm. of progesterone dissolved in 4 ml. of acetone were added. The speed of circulation of the broth was 250 ml./min. At 6, 8, 10, 12, 14, 16 and 18 hr. after the addition of progesterone, 250-ml. portions of the fermentation broth were drained off through the lower stopcock (4) and the same quantities of fresh broth added. The 6, 8 and 10 hr. portions contained 40 mgm. progesterone each, consequently a total of 280 mgm. of progesterone was added. The experiment was stopped after 20 hr. The broth samples were shaken with twice their volume of dichloroethane, the mycelium globules (5) retained in the column were extracted twice with 10 ml. of acetone and three times with dichloroethane, using 100 ml. of this solvent altogether. The extracts were washed with a 2 per cent solution of sodium bicarbonate, then with water, dried with sodium sulphate and, finally, investigated quantitatively by paper chromatography[2].

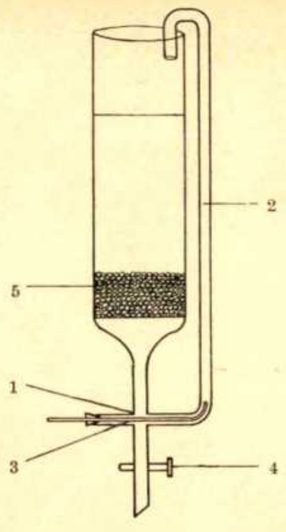

Fig. 1

Table 1

Sample taken at (hr.)	Contents of 11α-oxyprogesterone (mgm.)	Progesterone (mgm.)
6	58·8	—
8	51	—
10	35·6	—
12	33·8	—
14	30	—
16	21·8	—
18	9·7	—
20	3·7	—
From mycelium	0	38
Total	244·4	

Total recovery of steroids, 282·4 mgm.; conversion yield, 86 per cent

The results in Table 1 demonstrate the advantages of the method employed. The uncontaminated transformation product can be obtained from the fermentation broth, and the unchanged substrate recovered separately from the mycelial tissues. No loss occurs since the small quantity of untransformed progesterone can be totally recovered. The useful product is not subject to further oxidation since it is continuously extracted from the system. Tap-water can be used in place of the fermentation broth when changing the fluids ; in this case recovery becomes more simple still. The method can be used for all microbiological steroid conversions where the organism performing the transformation can be grown in pellet form and the polarity of the substrate molecule to be converted is not such as to make it soluble in the aqueous fermentation broth. Further, by this microbiological method, one of the great inconveniences of the fermentation process is obviated : it is not necessary to extract the final product from the whole broth, which may contain a number of undesirable contaminating substances.

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A Rare Sperm Abnormality : 'Corkscrew-sperms' associated with Sterility in Bulls

Williams and Savage[1] introduced a semen examination method for the evaluation of the seminal micropathology in bulls, the results of which in the hands of the experienced examiner are of definite value in sterility work, especially in classifying the severity of testis degeneration and testis hypoplasia. Later investigators have used slightly different systems for classifying abnormal sperm forms, but most workers have included abnormalities of the middle piece of the sperm in their counting as rather rare forms[2–4].

In 100 normal fertile bulls which I examined in 1950, by counting 500 sperms from each case, middle piece defects were only demonstrated in 0·27 per cent of the primary sperm abnormalities. Furthermore, in a long series of semen slides from cases of sterility in bulls examined by me during the past 15 years, middle piece abnormalities were never found as the main defect.

It was therefore of great interest to receive, within a period of a few months, from different parts of the country, abnormally thin semen samples from two sterile bulls showing almost the same morphological picture : most of the sperm heads were normal, but a high percentage of the sperms had middle pieces shaped like a corkscrew (Fig. 1), an abnormality which I had previously regarded as a curiosity.

By ordinary microscopy (× 1,000) the corkscrew sperms were easily seen and counted in slides stained with eosin–nigrosin[5] (Fig. 1*c*). In simple wet preparations also the abnormality was clearly distinguishable, especially by phase-contrast (Figs. 1*a* and *b*). None of the abnormal sperms was motile and none of them remained unstained (alive-reaction) with eosin–nigrosin.

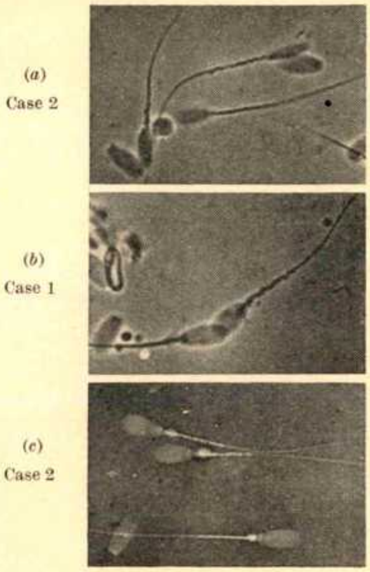

Fig. 1. Photographs showing typical corkscrew-sperms together with apparently normal sperms (× 600). (*a* and *b*) Phase-contrast exposures from wet preparations ; (*c*) a slide stained with eosin–nigrosin

Case 1. RDM bull, 5 years old. Until December 1957 the bull was used regularly at an artificial insemination centre. Semen quality and fertility : fair. Dilution rate : generally 1 + 2 only. From January 1958 semen quality was going down, motility almost nil and concentration decreasing rapidly, so the bull was taken out of use. Clinical examination, July 1958 : testis normal sized, probably with some fibrous induration.

Table 1

Date of semen examination	Motility (per cent)	Sperms/mm.^{3}	Corkscrew sp. (per cent)
Aug. 27, 1958	<1	40,000	24
Sept. 2, 1958 (I)	<1	100,000	15
Sept. 2, 1958 (II)	<1	50,000	16

Diagnosis : Testis degeneration, cause unknown.

Unfortunately this bull was sent for slaughter without further examination being made.

Case 2. RDM bull, 12 years old. Has belonged to the same artificial insemination centre for about 11 years. During the first 9 years the bull was used regularly three times weekly and always had semen of top quality and high fertility. When the bull was about 10 years old sperm concentration decreased somewhat and fertility dropped to fair. From April 1958 the semen was practically dead and of low concentration (last successful insemination March 1958). This bull is still alive.

Table 2

Date of semen examination	Motility (per cent)	Sperms/mm.^{3}	Corkscrew sp. (per cent)
Oct. 22, 1958 (I)	<1	200,000	23
Oct. 22, 1958 (II)	<1	100,000	27
Nov. 5, 1958	<1	200,000	31
Nov. 19, 1958	<1	75,000	45
Dec. 1, 1958	<1	75,000	49

Diagnosis : Testis degeneration, cause unknown.

The occurrence of characteristic corkscrew sperms with twisted middle pieces in 15–49 per cent by the differential sperm count in two sterile bulls (primarily fertile) seems to indicate the existence of a hitherto rare form of testis degeneration, where the specific blastema for the middle piece, including the so-called mitochondrial sheet, is affected.

Of these two sterile bulls it was only possible to follow one during a short period before slaughter, while semen samples from the other were examined during some months, showing that the occurrence of corkscrew-sperms increased regularly, from 23 to 49 per cent, while, as a decrease in sperm concentration indicated, degeneration of the testis tissue was in progress.

Only Bretschneider[4] (drawing 114) seems to have encountered a similar phenomenon, with a sort of macrohelix-structure in the middle pieces in 20 per cent of the sperms, but unfortunately no photographs and no information about the fertility of the bull in question are given. These results seem to indicate that investigators who are doing morphological sperm examinations for fertility in bulls should pay full attention to the condition of the middle pieces, and in future work also include corkscrew-sperms in the group of primary sperm abnormalities.

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Hair as a Substrate for Non-Keratinolytic Fungi

DURING a study of the fungal succession occurring on hair decomposing in contact with soil, it has become apparent that hair, either autoclaved or sterilized with propylene oxide, can support the limited growth of many fungi which are not keratinolytic. Thus species of *Mortierella*, *Cunninghamella* and *Chaetomium*, as well as of many genera of the Fungi Imperfecti, for example, *Aspergillus*, *Gliocladium*, *Penicillium*, *Alternaria*, *Curvularia*, *Epicoccum*, *Helminthosporium*, *Phoma*, *Pyrenochaeta*, grow sparsely on the hair surface and produce spores there.

The ease with which such fructifications can be examined has led to the use of hair as a fungal substrate for class purposes while teaching mycology. Fine human hair, sterilized either by autoclaving at 15 lb. pressure for 15 min. or with propylene oxide[1], is placed on the surface of a thin layer of agar of low nutrient status contained in a Petri dish, and the agar is inoculated with the fungus to be studied. Within a few days, the mycelium has spread from the agar to colonize sparsely the hair surface, and scattered conidiophores are produced. A hair is then carefully removed with forceps and mounted on a slide in any suitable mounting fluid. The preparation, under a cover-slip, can then be readily examined under a microscope. The great advantage of the method lies in the ease with which an inexperienced worker can obtain an undisturbed preparation of conidiophores and conidia, clearly revealing the exact method of production of the latter, a detail which is assuming an increasing importance in taxonomy[2]. Although the mode of production of conidia remains typical, the poverty of hair as a substrate for the majority of fungi occasionally leads to a simplification in conidiophore morphology. Thus in the genus *Penicillium*, the penicillus is frequently of a simpler nature than the corresponding structure produced on an agar medium, so that the hair technique is not satisfactory when specific identification is attempted in such genera.

The method has also proved advantageous in promoting either the asexual reproduction of apparently sterile cultures or the production of more easily characterized structures in those cultures which produce nothing but an ill-defined mass of simple slime spores on the normal agar media. In many cases cultures of either of these types have readily produced pycnidia on the hair surface.

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Discoloration of Wool Fibres by a Fungus

A COMPLAINT by a wool processer in Japan that part of a consignment of New Zealand raw fleece wool in the coarse-quality range was affected by a black discoloration which could not be removed in the ordinary wool scouring process, or by any common solvent, has been investigated and the cause of the discoloration established as being due to a fungus growing in the fibres.

In outward appearance the distal part of the staple was dark coloured and similar in appearance to wool contaminated by dust and dirt. All parts of the fleece appeared to be equally affected. On scouring or after solvent-treatment the affected staple tip remained dark. In the region of discoloration, fibres had a very low tensile strength characteristic of extreme weathering.

Microscopic examination showed the fibre to be outwardly intact. Large fungal hyphæ were obvious within the fibre and cross-sections showed a severe mechanical disruption of cortical cells within the fibre, this no doubt contributing to the loss of tensile strength. Within the fibre the hyphæ are moniliform in shape and dark in colour. At irregular intervals the hyphæ anastomose and fruiting structures are formed which finally reached the surface by breaking through overlying cortical and cuticular cells of the fibres. Minute hyaline ellipsoidal unicellular or two-celled spores are produced in these structures.

The fungus was isolated from affected wool by placing short lengths of the infected fibres on tryptone glucose extract agar ('Difco') to which 0·01 gm./ml. of 'Terramycin hydrochloride' had been added aseptically just prior to pouring the plates. The fungus, which grew out readily, was transferred to slants of the same medium, where it formed fruiting bodies profusely. The fungus is reported by the Commonwealth Mycological Institute to be a species of *Peyronellaea*, not recorded from wool but close to *Peyronellaea glomerata* (Corda) Goidanich, and has been disposed in the Commonwealth Mycological Institute herbarium as *I.M.I.* 74752.

No reports of fungus damage to unprocessed wool have been found in the literature, although several unidentified actinomycetes have been shown to be capable of bringing about a rapid disintegration of wool fibres while still on the sheep[1], and this present report indicates a further source of damage by a group of organisms that has been little studied in relation to the fleece.

Further investigations into the methods of spread of the fungus and its infection of wool are in progress and a full account will be published elsewhere.

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Abnormal Development of the Basis in *Balanus amphitrite* var. *stutsburi* Darwin

The deformation of barnacle shells by growth on unfavourable substrates is now well known[1,2]. The distinctive scalloped form of basis produced on toxic anti-fouling paints has been illustrated by these and other authors. The same deformity occurs when settlement takes place on a toxic metal surface, for example, the copper sheathing of a wooden hull.

Recent examination of some specimens of *Balanus amphitrite* var. *stutsburi* Darwin from "West Africa" in the City Museum, Bristol, dating from the mid-nineteenth century and conceivably belonging originally to Samuel Stutchbury, showed that four of the five specimens handled have this deformed basis (Fig. 1). The fifth is regular in outline except where distorted by two small encrusting oyster shells. Spectrographic examination of green material in the crevices of the contorted bases indicated a high percentage of copper. No copper was associated with the other smooth-shelled specimen. Nor was any found in the glue used to secure the specimens to the display 'tablet'. It is practically certain therefore that the deformed specimens are derived from the bottom of a copper-sheathed ship on which they arrived in Great Britain, presumably from West Africa, the home of this variety.

In the Darwin cirripede material in the British Museum (Natural History) there are mounted on a tablet, among other named varieties, eight numbered specimens assigned to *B. a. stutsburi* in a manuscript list in Darwin's hand. Of these, five are distorted specimens, one (No. 18 on the tablet) possibly the original of Darwin's illustration of the variety (Pl. V, Fig. 2*d*)[3]. Thus Darwin illustrated a deformed specimen only while also having normal material before him. This is still the only illustration of the complete shell of *B. a. stutsburi*.

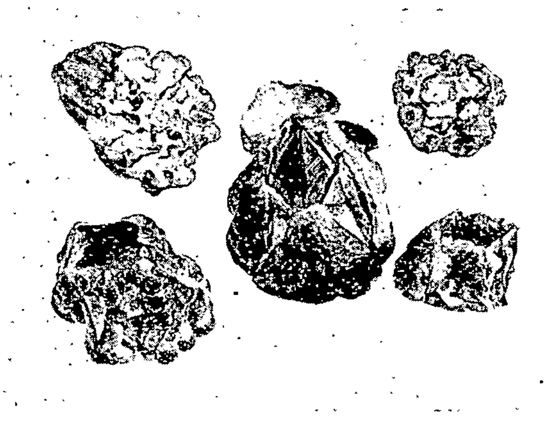

Fig. 1. *B. amphitrite stutsburi* Darwin. Four deformed specimens from a copper substrate and one normal smooth-walled specimen. (Bristol City Museum Collection)

Current examination of a large collection of new material of the variety from West Africa has shown that the rugged or deformed type figured by Darwin does not occur on natural and non-toxic substrates, for example, shells, stones, wood, concrete and iron, and that *stutsburi* is normally a smooth variety of *B. amphitrite* in its natural habitat.

The form and variability of this and some other varieties of *B. amphitrite* will be discussed at greater length in subsequent papers to be published, in collaboration, elsewhere.

I am indebted to the Director, City Museum, Bristol, for the loan of the specimens figured here, to my colleague, Mr. L. G. Young, for the spectrographic examinations of the copper-containing inclusions from the bases, and to the Director, British Museum (Natural History), for permission to examine the Darwin and other material in that Museum.

H. G. Stubbings
Admiralty Materials Laboratory,
Holton Heath,
Poole, Dorset.
Feb. 24.

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[2] Weiss, C. M., *Ecology*, 29, 116 (1948).

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A Quantitative Serum–Agar Technique

While investigating the changes which occur in plant cytoplasmic proteins during growth and differentiation, using the Ouchterlony serum – agar plate technique[1], the need arose for a quantitative method of estimating the protein constituents. Although there are several methods available[2–7], none of them is easily applicable to a multi-antigenic system, and in addition the concentrations of the proteins can only be estimated separately, even under favourable conditions, at ±10 per cent and more usually ±50 per cent.

With the method described here it has been possible, with the system studied, to estimate the relative protein concentration within ±4 per cent, and it is probable that the technique could be developed to limits of ±2 per cent. The sensitivity of the technique is dependent on at least three factors: standardization of procedure; the titre of the individual protein or proteins; and the accuracy with which one can pipette the small volumes of liquid which have to be used when the antiserum, and sometimes the antigen solution, is in short supply.

The method consists of titrating antigen on to antibody and following the titration on a modified Ouchterlony plate. Two end-points are obtained (Fig. 1): (*a*) where free antibody is just detectable; (*b*) where free antigen is just detectable.

The technique is as follows: into a series of small tubes is pipetted a standard volume of antiserum (0·1 ml. of monospecific siderophilin antiserum was used in these experiments). To each of these is added the same volume of antigen in a series of different concentrations (normal human serum diluted

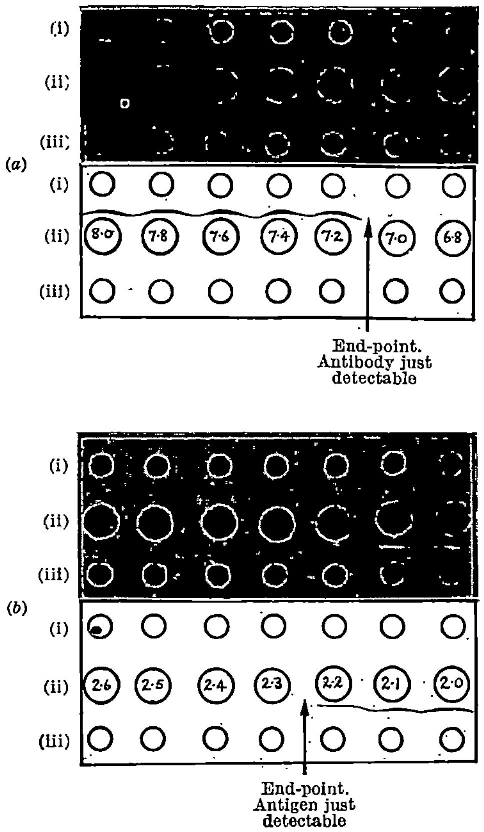

Fig. 1. The determination of the two end- or extinction-points for siderophilin: *a*, where free antibody is just detectable; *b*, where free antigen is detectable. (i) Total human serum diluted × 8; (ii) monospecific siderophilin antiserum absorbed with a range of concentrations of total serum; the figures indicate the dilution of the antigen; (iii) the above antiserum diluted × 4

with physiological saline). The antibody and antigen are allowed to react for 2 hr. at 37° C. and then agar plates are set up as shown in Fig. 1 (0·6 per cent w/v New Zealand agar in veronal buffer, pH 8·6 (sodium diethylbarbiturate 0·1 M; diethylbarbituric acid 0·02 M)) using equal volumes of absorbed antiserum in each well and similarly for unabsorbed antiserum and antigen. The plate is incubated at 37° C. for 20 hr. and the end-point determined visually. (37° C. was used for both the initial reactions and for the end-point detection test; in certain circumstances, especially with weak antiserum, periods at 0° C. might be preferable.)

This experiment describes the determination of the two end-points for a standard antigen solution when used in conjunction with a particular antiserum. To estimate the concentration of the antigen in an unknown solution it would be necessary to determine only one of the two end-points (preferably the sharper, usually, as in this instance, the one where antigen is just detectable) and to express it in arbitrary units based on the standard. In the rare event of a pure antigen being available the end-point could be expressed as mgm. protein.

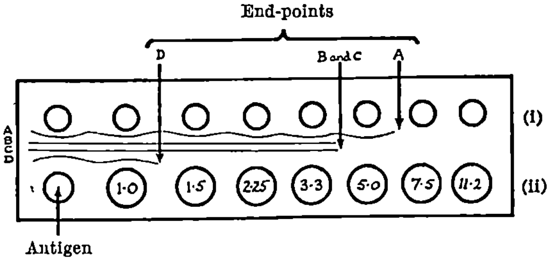

Fig. 2. Hypothetical example of the determination of the end-points (that is, where free antigen is just detectable) of a multiple protein system: (i) antiserum; (ii) antiserum absorbed with a range of concentrations of antigen. The figures indicate the dilution of the antigen

On theoretical grounds the end-point where antigen is just detectable is likely to be the more sensitive, because it is favoured by the shape of the precipitation curve, which is usually not symmetrical about the equivalence point, and because a small amount of antigen is more easily detectable than a small amount of antibody. Using this end-point for a multiple protein system several lines can be identified by setting up a plate as shown in Fig. 2, which shows a hypothetical example of the simultaneous estimation of all four antigens.

I wish to thank Prof. J. R. Squire for his encouragement and advice and Dr. P. G. H. Gell for his constructive criticisms.

The work was carried out under a grant from the Nuffield Foundation.

S. T. C. Wright

Department of Experimental Pathology,
Medical School,
University of Birmingham.

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[4] Oakley, C. L., and Fulthorpe, A. J., *J. Path. Bact.*, **65**, 49 (1953).

[5] Augustin, R., and Hayward, B. J., *Int. Arch. Allergy*, **6**, 154 (1955).

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[7] Gell, P. G. H., *J. Clin. Path.*, **10**, 67 (1957).

Photographic Recording of Agar Diffusion Plates

A NUMBER of requests have been received at this Establishment asking for details of the method and materials used for the photographic recording of agar diffusion plates[1-4]. It may be of help to those using the Ouchterlony[5] and Mansi[6] techniques if the successful system devised and regularly in use here is made more widely known.

It was found that the greatest contrast, both visual and photographic, between the lines of precipitation and the background, is obtained when the beam of transmitted light is as nearly as possible normal to the agar surface, without the source itself being visible to the eye or the lens. The apparatus shown in Fig. 1 is one of the most compact and stable arrangements which will fulfil this condition. The bright aluminium sheet serves to reflect excess light and heat from the 500-watt spotlights, and has a circular aperture a little larger than that of the blackened dish support, which is separated from it by washers as spacers to prevent heat transfer. Standard 9-cm. Petri dishes are generally used, but a series of metal annuli, blackened on top and bright underneath, having 9-cm. outside diameters and three registering pegs set equilaterally around the inside diameters, support smaller dishes centrally over the aperture, and at the same time exclude excess light. Using a 13·5-cm. Tessar lens, 9-cm. dishes are photographed at a small degree of direct enlargement (to

11 cm.) on quarter-plate cut film. A stop of $f/8$ gives sufficient depth of field to bring the whole thickness of agar into focus. With high-contrast film (Ilford 'Ortholine', *G*5.51) and an exposure time of 1/50 of a second, 5 min. development in a standard phenidone-quinone developer (Ilford *I.D.* 62) allows adequate contrast, without blocking up the finer and fainter lines.

As the plane of light falling on the Petri dish tends to be diametral, separation of a close-running 'family' of lines, particularly where strong and faint ones are adjacent, is greatest when their direction is set parallel to that plane, as otherwise the scatter of light from the heavy lines may overshadow the finer ones. Lines of a circular precipitation zone around a cup are well differentiated even when at right angles to the light plane ; this is not always the case with fully annular lighting, such as that from a Quebec colony counter, in which the rays are much nearer parallel to the agar surface.

Since this method of lighting was designed to accentuate the faintest lines to the greatest possible degree against a dark background, it follows that dust and fibres on the agar, and scratches on the bottom of the Petri dish, are also brought into prominence. Debris on the surface can be kept to a minimum by care taken when the dish is opened for inspection of the lines. Scratches and irregularities on the bottom of the Petri dish can be removed effectively, for the purpose of photography, by temporarily 'cementing' the dish to a scratch-free and flawless glass disk of suitable size with glycerine, avoiding the inclusion of air-bubbles.

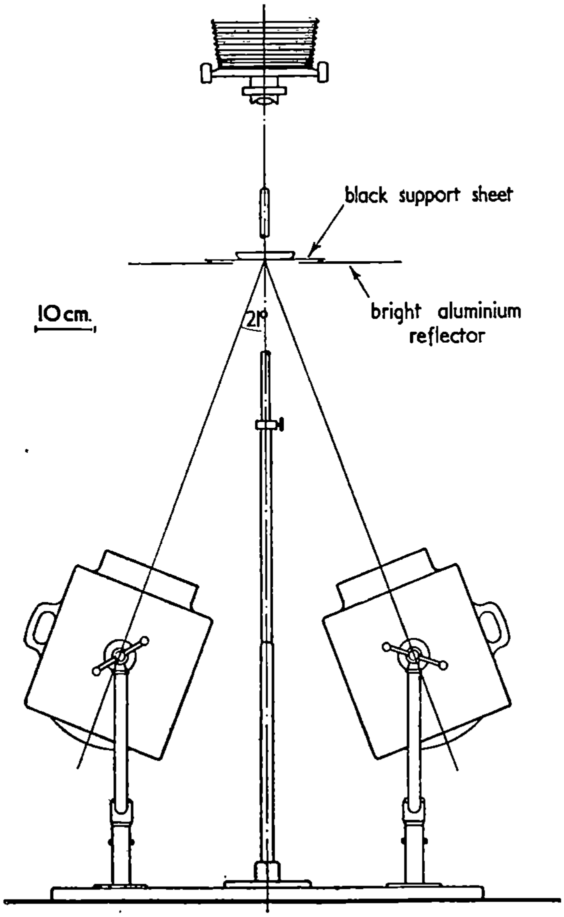

Fig. 1. Diagram of apparatus

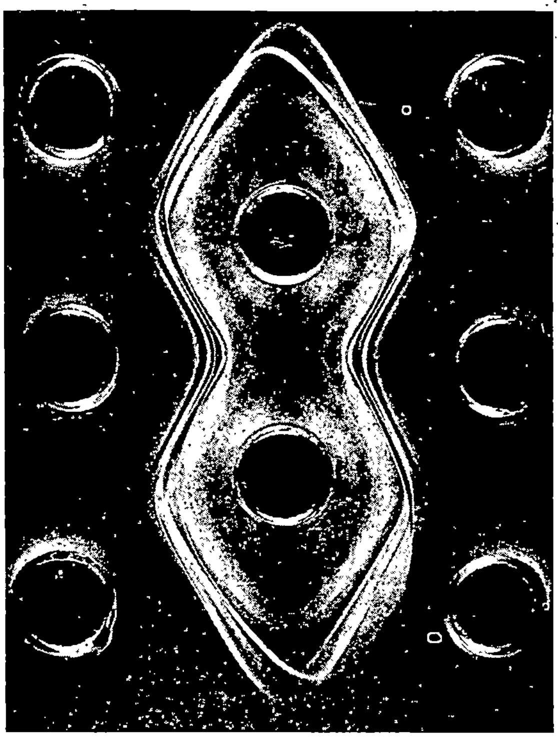
[*Crown copyright reserved*

Fig. 2. Routine record of a *Pasteurella pestis* antigen–antibody system

In order that the equipment may be used for routine recording by staff who are not trained photographers, the number of variables has been kept to the absolute minimum. The camera, which is also used in conjunction with other equipment, is fixed to the wall, and has register marks on the adjustable stays. The spotlights and dish support, in one unit on a baseboard, are centred under the lens by means of spacing-rods to the wall. Negative processing is standardized by time and temperature. The greater degree of direct enlargement of smaller Petri dishes is compensated for in the normal way by an increase in exposure time, but is not often needed. There is sufficient latitude, even with the high-contrast emulsion used, normally to cover the amount of variability inherent in the diffusion plates themselves and good-quality negatives are obtained with the standard exposure time. Very little practice is needed to learn when slight adjustments will be required.

Two years experience has shown that the faintest of lines can be recorded with ease, and with an accuracy and saving of time much greater than is obtainable when the lines are recorded by drawing.

J. R. Hunter

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Experimental Station,
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Feb. 6.

[1] Burrows, T. W., and Bacon, G. A., *Brit. J. Exp. Path.*, **37**, 490 (1956).
[2] Davies, D. A. L., *Biochem. J.*, **63**, 105 (1956).
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[5] Ouchterlony, O., *Ark. Kemi, Min., Geol.*, **26**, B, 1 (1949).
[6] Mansi, W., *J. Comp. Path.*, **67**, 297 (1957).

FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Monday, May 4

Faraday Society (at the Imperial College of Science and Technology, South Kensington, London, S.W.7), at 4.30 p.m.—Dr. Robert Gomer (University of Chicago): "Surface Diffusion" (Bourke Lecture).*

London School of Economics and Political Science (at Houghton Street, Aldwych, London, W.C.2), at 5 p.m.—Prof. M. J. Wise: "Industrial Location—a Geographical Approach"* (Inaugural Lecture).

British Society for the History of Science (in the Council Room of the Science Museum, Exhibition Road, South Kensington, London, S.W.7), at 5.30 p.m.—Dr. Churchill Eisenhart: "The Background and Evolution of the Methods of Least Squares".

Society of Engineers (at the Geological Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Mr. D. J. Ayres: "Grouting and the Civil Engineer".

University of London (in the Large Chemistry Theatre, Royal College of Science, London, S.W.7), at 5.30 p.m.—Prof. W. Lochte-Holtgreven: "Magnetic Fields in Rotating Plasma".* (Last of three Special University Lectures on "Spectroscopic and Magnetic Studies of Thermally Excited Plasmas".)

Royal Society of Arts (at John Adam Street, Adelphi, London. W.C.2), at 6 p.m.—Mr. J. R. Whinfield: "Research in Man-made Fibres". (Last of three Cantor Lectures.)

Society of Chemical Industry, London Section (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Annual General Meeting, followed by Mr. E. L. Streatfield: "The Conveyor Concept of Water in Industry".

Tuesday, May 5

Institution of Electrical Engineers, Measurement and Control Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Prof. A. L. Hodgkin, F.R.S.: "Propagation of Electrical Signals along Nerve Fibres".

University College (in the Anatomy Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. V. B. Mountcastle (Johns Hopkins University): "The Central Nervous Mechanisms in Somatic Sensation".* (First of two Special University Lectures in Human Anatomy and Morphology. Further lecture on May 7.)

University of London (at the Institute of Education, Malet Street, London, W.C.1), at 5.30 p.m.—Academician I. A. Kairov: "Education of Students in the Spirit of Patriotism, Peace and Friendship amongst the Nations".* (Further lecture on May 8.)

British Council, and the Joint Committee on Structural Concrete (at Friends' House, Euston Road, London, N.W.1), at 6 p.m.—Mr. Felix Candela: "Ten Years Building Thin Shell Structures".

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Prof. F. E. Zeuner: "The Origins of Domestication—a Synthesis".* (First of six lectures on "Animals in Archæology". Further lectures on May 12, 19, 26, June 2 and 9.)

British Institution of Radio Engineers (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Mr. I. M. Ross, Mr. C. P. Lea-Wilson, Mr. A. J. Monk and Mr. A. F. H. Thomson: "An Experimental Diode Parametric Amplifier and Its Properties".

Plastics Institute, London and District Section (at the Wellcome Building, 183–193 Euston Road, London, N.W.1), at 6.30 p.m.—Annual General Meeting. Mr. C. Shaw: "Precision Cast Moulds and Tools for the Plastics Industry".

Society of Chemical Industry, Plastics and Polymer Group (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—27th Annual General Meeting, followed by Mr. C. E. Hollis: "The Pursuit of Polymers" (Chairman's Address).

Royal Aeronautical Society (at 4 Hamilton Place, London, W.1), at 7 p.m.—Mr. R. H. Scott: "The Potential Use of Aircraft for Agricultural Purposes (with particular reference to New Zealand)".

Wednesday, May 6

Society of Dairy Technology (at the Federation of British Industries, 21 Tothill Street, London, S.W.1), at 10.30 a.m.—Meeting on "Some International Aspects of the Dairy Industry".

Institute of Petroleum (at 61 New Cavendish Street, London, W.1), at 5.30 p.m.—Symposium on "Submarine Exploration for Oil" presented by Members of B.P. Exploration Co., Ltd.

Society of Instrument Technology (at Manson House, Portland Place, London, W.1), at 5.30 p.m.—Annual General Meeting. 6.30 p.m.—Presidential Address.

University College, Department of Hebrew (in the Gustave Tuck Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. Theodor H. Gaster (Dropsie College for Hebrew and Cognate Learning): "New Light on the Dead Sea Scrolls".* (Further lecture on May 7.)

University of London (in the Small Physics Lecture Theatre, Royal College of Science, Imperial College of Science and Technology, Imperial Institute Road, London, S.W.7), at 5.30 p.m.—Prof. M. Biernacki (Marie Curie-Sklodowska University, Lublin): "Sur les Extréma des Combinaisons des Fonctions, Sous-Harmoniques et de leur Généralisations".*

University of London (at Bedford College, Regent's Park, London, N.W.1), at 6 p.m.—Prof. D. J. van Lennep (Utrecht): "Recent Studies on the Personality of the Proficient Research Worker". (Further lecture on May 7.)

Institution of Electrical Engineers, London Graduate and Student Section (at Savoy Place, London, W.C.2), at 6.30 p.m.—Annual General Meeting, followed by Films.

Society of Chemical Industry, Corrosion Group (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Annual General Meeting, followed by Dr. S. G. Clarke: "Corrosion as a Design Problem" (Chairman's Address).

Society for Analytical Chemistry (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Meeting on "The Design of Experiments in Analytical Chemistry". Dr. E. C. Wood: "The Fundamental Principles of Modern Experiment Design"; Mr. W. C. Wake: "Statistics in Standardizing Chemical Methods".

Society for Visiting Scientists (at 5 Old Burlington Street, London, W.1), at 7.30 p.m.—Discussion Meeting—"As Others See Us". Chairman: Prof. A. V. Hill, F.R.S. Speakers: Dr. C. Kemal Reheem: "Some Views from Pakistan on British Science"; Dr. Thomas H. Osgood: "The American View"; Mr. A. C. Copisarow: "Impressions from Some West European Countries".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. David R. Newith: "Black Axolotl, and White".

Wednesday, May 6—Thursday, May 7

Iron and Steel Institute (at Church House, Westminster, London, S.W.1), at 10 a.m. daily—Annual General Meeting.

Thursday, May 7

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Prof. W. T. J. Morgan, F.R.S.: "A Contribution to Human Biochemical Genetics: The Chemical Basis of Blood Group Specificity" (Croonian Lecture).

Linnean Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. K. Mather, F.R.S., and Dr. J. A. Roper: "Cytoplasmic Inheritance"; Mr. W. T. Stearn: "Baron von Humboldt (1769–1859)".

London School of Economics and Political Science (at Houghton Street, Aldwych, London, W.C.2), at 5 p.m.—Mr. T. H. Marshall: "International Comprehension in and through Social Science"* (Hobhouse Memorial Lecture).

Institute of Refrigeration (joint meeting with the Low Temperature Group of the Physical Society, at the Memorial Building, 76 Mark Lane, London, E.C.3), at 5.30 p.m.—Mr. D. Hurden: "Cryogenic Liquids for Rocket Engines".

Institution of Electrical Engineers, Utilization Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. J. M. Waldram: "Lighting and Architecture".

Royal Anthropological Institute (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Dr. Phyllis Kaberry: "Nsaw Political Conceptions".

University of London (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. François Jacob (Institut Pasteur, Paris): "Viruses in Relationships with some Genetic Elements of the Cell".*

Polarographic Society (at "The Duke of York", 8 Dering Street, London, W.1), at 7 p.m.—Informal Discussion Meeting on "Some Problems Encountered in Anodic Polarography".

Chemical Society (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Scientific Papers.

Friday, May 8

Aslib (in consultation with the British Association of Industrial Editors, the North-Western Polytechnic, and the Presentation of Technical Information Group (at the Connaught Rooms, Great Queen Street, Kingsway, London, W.C.2), from 10.30 a.m. to 5 p.m.—Conference on "The Presentation and Interpretation of Technical Information".

Royal Astronomical Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Prof. H. H. Plaskett: "Solar Rotation and Photospheric Circulation"; Dr. M. J. Seaton: "The Calculation of Recombination Spectra".

Institution of Electrical Engineers, Medical Electronics Discussion Group (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Microwave Radiation Hazards", opened by Dr. D. H. Shinn and Dr. N. L. Lloyd.

University of London (at the Royal Holloway College, Englefield Green, Surrey), at 8.15 p.m.—Sir Edward Salisbury: "The Royal Botanic Gardens, Kew, 1759–1959".

Friday, May 8—Saturday, May 9

British Society for Immunology (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1)—Spring Meeting.

Friday, May 8, at 11 a.m.—Symposium on "Delayed Hypersensitivity". Chairman: Prof. G. Payling.

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Lecturer in the Department of Biochemistry—The Secretary, The University, Edinburgh (May 9).

Senior Lecturer in the Department of Biochemistry—The Secretary, The University, Edinburgh (May 9).

Junior Biochemist (with an honours degree)—The Secretary, Institute of Animal Physiology, Agricultural Research Council, Babraham, Cambridge (May 15).

Junior Lecturer/Lecturer in Physiology—The Secretary, The London Hospital Medical College (University of London), Turner Street, London, E.1 (May 15).

Research Assistant (Physical Chemist), for work with organometallic compounds—The Secretary, The University, Exeter (May 15).

Foresters (2) (with a Diploma or a Certificate of a recognized foresters' training school and preferably aged between 20 and 25) on the Staff of the Southern Rhodesia Forestry Commission—The Secretary (R), Rhodesia House, 429 Strand, London, W.C.2 (May 16).

Lecturer or Assistant Lecturer (interested in the mechanisms of reactions) in the Department of Organic Chemistry—The Registrar, The University, Liverpool (May 16).

Map Curator (preferably geography graduate with an interest in maps and bibliographic work) in the Department of Geography—The Registrar, The University Leeds 2 (May 16).

Lecturer (with qualifications in physical science or mathematics) in the Department of Education—The Registrar, University College of Wales, Aberystwyth (May 18).

Assistant Lecturer in Metallurgy—The Registrar, The University, Nottingham (May 23).

Assistant Lecturer (with a good honours degree in chemistry or agricultural chemistry) in Agricultural Chemistry—The Registrar, The University, Leeds 2 (May 23).

Research Assistant (with a good honours degree in botany or biochemistry or chemistry) in the Department of Botany, to assist in research on the mechanism of photosynthesis—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (May 23).

Assistant Lecturer (with an honours degree in agriculture, animal physiology or animal nutrition, or a pass degree in agriculture with a suitable postgraduate diploma, or equivalent qualifications) in Agriculture (Animal Husbandry)—The Registrar (Room 22, O.R.B.), The University, Reading (May 30).

Assistant Lecturers (honours graduates) in Physics and Zoology—The Secretary, Bedford College (University of London), Regent's Park, London, N.W.1 (May 30).

Esso Research Student (with, or expecting to hold, a good university degree with chemistry as the principal subject) in Chemistry—The Professor of Chemistry, The University, Southampton (May 30).

Lecturers and Assistants in Experimental Physics, Theoretical Physics, and Electronics, in the Natural Philosophy Department—The Secretary, The University, Aberdeen (June 1).

Reader in Pharmacology at Middlesex Hospital Medical School—The Academic Registrar, University of London, Senate House, London, W.C.1 (June 1).

Chair of Biology as applied to Medicine tenable at the Middlesex Hospital Medical School—The Academic Registrar, University of London, Senate House, London, W.C.1 (June 2).

Lecturer/Senior Lecturer (preferably interested and with research experience either in Western industrial societies or in Africa) in Anthropology, University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 6).

Research Fellows (2) in the Department of Anthropology and Sociology, Research School of Pacific Studies, Australian National University, to carry out and assist in the supervision of research in social anthropology and sociology amongst primitive and advanced peoples in Australia and neighbouring parts of the world—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 15).

Assistant Lecturers (2) in Zoology—The Principal, Royal Holloway College (University of London), Englefield Green, Surrey.

Biochemist (with an honours degree in chemistry or biochemistry, and preferably research experience) in the Chemistry Department, to carry out research on trace elements in relation to diseases of farm animals—The Secretary, Animal Diseases Research Association, Moredun Institute, Gilmerton, Edinburgh 9.

Chair of Applied Mathematics; Associate Professor; and an Assistant Professor in the Department of Mathematics—Prof. H. H. Ferns, Department of Mathematics, University of Saskatchewan, Saskatoon, Sask., Canada.

Demonstrator in Pharmaceutics, and a Demonstrator in Pharmaceutical Chemistry—The Registrar, The University, Nottingham.

Master to teach Physics to "A" or preferably "S" level—The Headmaster, Westminster School, 17 Dean's Yard, London, S.W.1.

Research Assistant (with a degree or equivalent qualification in chemistry), for work on physico-chemical problems at high temperatures—Dr. J. W. Tomlinson, Royal School of Mines, Prince Consort Road, London, S.W.7.

Research Engineers (2) (with at least an honours degree in mechanical engineering, or in some other specialization covering fluid mechanics) in the Department of Aircraft Propulsion, for theoretical and experimental work on the fluid mechanics of gas flow in solid rocket motors—The Recorder, The College of Aeronautics, Cranfield, Bletchley, Bucks.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Royal Society. British National Committee for the International Geophysical Year. United Kingdom Antarctic Report to the Fifth C.S.A.G.I. Meeting (Moscow 30 July–9 August 1958). Pp. 20. (London: Royal Society, 1958.) [272

The Manchester Museum. Report of the Committee for the year ending July 31st, 1958. Pp. 20. (Manchester: The Manchester Museum, The University, 1959.) [272

The Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research. Report for 1958. Pp. 52. (London: Ciba Foundation, 1959.) [272

Language, Literature and Science: an Inaugural Lecture. By Prof. A. Norman Jeffares. Pp. i+24. (Leeds: The University Press, 1959.) 2*s.* 6*d.* [272

Department of Scientific and Industrial Research. Memoirs of the Geological Survey of Great Britain. England and Wales. Geology of the Country around Bridport and Yeovil (Explanation of Sheets 327 and 312). By Dr. Vernon Wilson, Dr. F. B. A. Welch, J. A. Robbie and G. W. Green. With contributions on The Purbeck Beds by Dr. F. W. Anderson. Palaeontology by R. V. Melville. Ground Water by Dr. S. Buchan. Pp. xii+239+7 plates. (London: H.M. Stationery Office, 1958.) 30*s.* net. [272

Bulletin of the British Museum (Natural History). Zoology. Vol. 5, No. 7: The Monotypic Genera of Cichlid Fishes in Lake Victoria, Part 2; and a Revision of the Lake Victoria *Haplochromis* Species (Pisces Cichlidae), Part 3. By P. H. Greenwood. Pp. 163–218. 16*s.* Vol. 5, No. 8: The *Rosaura* Expedition 1937–38. Chaetognatha. By John S. Colman. Pp. 219–253. 12*s.* Vol. 5, No. 9: A North Bornean Pygmy Squirrel, *Glyphotes simus* Thomas, and Its Relationships. By J. E. Hill. Pp. 255–266+plates 7 and 8. 7*s.* (London: British Museum (Natural History), 1959.) [272

Other Countries

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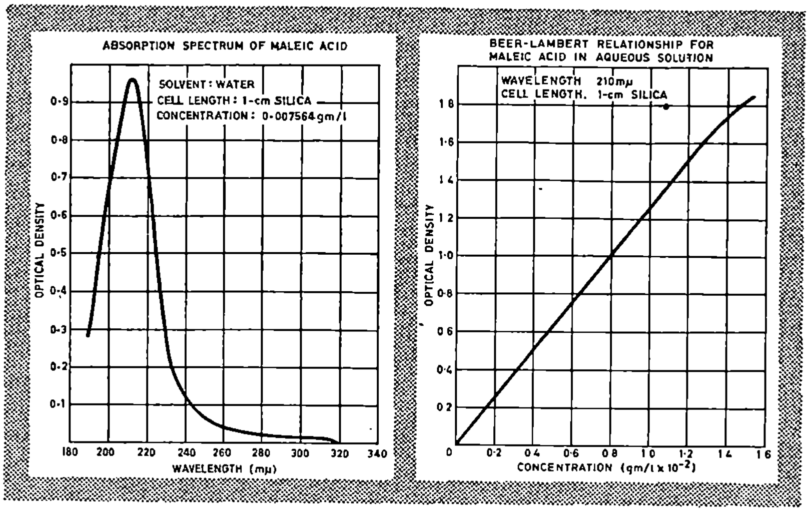

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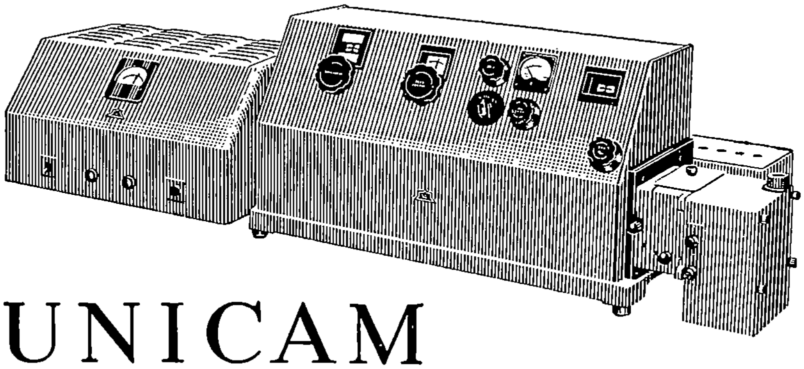

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LIBRARY SERVICES IN BRITAIN

IN its report[*] on "University Development, 1952–1957", the University Grants Committee pointed out that much university expenditure for research is expenditure on libraries, but although it is possibly true that libraries are relatively more important to the arts and related subjects than to the sciences—it has been estimated that library expenditure per arts student is double that on other students—the importance of efficient and adequate library service in science and technology is not easily over-stressed. The University Grants Committee did not discuss library expenditure exclusively in relation to research in the humanities and the social sciences; but in this report, although it recognized the constantly increasing pressure on university libraries, it did not emphasize the importance of the library itself as a factor in university education in general. Library expenditure increased by 64 per cent between 1951–52 and 1956–57, but is still only 3·9 per cent of university expenditure compared with 3·8 per cent in 1951–52, whereas full-time students have increased from 83,458 to 89,866 and academic staffs from 8,952 to 10,485; by 1961–62 the number of students is now expected to rise to 110,000 or more. Readers' places in university libraries increased by 17 per cent between 1953–54 and 1956–57, from 17,895 to 20,938; but the increase is unevenly spread, and in some universities the position is getting worse. Moreover, the 37 per cent increase in the cost of books, periodicals and bindings between 1951–52 and 1955–56 has reduced the real increase in library expenditure to something less than 10 per cent.

Although the University Grants Committee reports that capital works to cost about £1·75 million have been started in seven universities in Britain, there is no note of real urgency in its report. According to F. E. Hirsch, the Association of College and Research Libraries now recommends that the library should receive 5–7 per cent of the total educational budget of an institute. At the Home Universities Conference last December, Prof. R. J. Pumphrey advocated doubling the library allocation and instituting a three-year plan with the object of guaranteeing to every undergraduate access at very short notice to any book he is likely to want and a place in which to read it as one means of meeting the pressure which the forthcoming expansion is likely to put upon the universities. It may be doubted whether doubling the present expenditure of £1,620,978 is anything like enough to achieve this object, and Prof. Pumphrey gave no indication of the capital expenditure that would be involved. To provide libraries of 40,000 volumes for every 600 students, with a further 10,000 for every 200 students up to, say, 300,000 volumes, as suggested by the Association of College and Research Libraries, is a major task demanding financial resources which neither the University Grants Committee nor the Ministry of Education or local authorities appear at present to be contemplating. Indeed, the expansion of university libraries, within the limits of any foreseeable resources that are likely to be made available, may need planning with some regard to the requirements of the colleges of technology and the technical colleges, if only from the point of view of the very close co-operation demanded by the Association of College and Research Libraries Committee on Standards. All are affected, too, by the presence of students coming from homes where there is no tradition of books but rather Ruskin's "abyss of penury", and who have not learned the value of possessing and cherishing even a few well-chosen books, and are unprepared to make the sacrifice that such purchase may entail.

In practice, it is probably only within the framework of an efficient and reasonable regional public library system that the needs of even the university student are likely to be met from the resources which the universities will be able to devote to library services within the next decade. These services, as already indicated, have to meet the needs of research workers, quite apart from the invaluable contribution which the universities themselves have long made to the national lending library system in Britain. The universities must thus be vitally interested in any proposals for the development of a national reference library or a national lending library for science and technology, just as the scope and content of any such libraries should be planned with some regard to regional needs and resources if duplication and waste of effort and resources are to be avoided.

It is in accordance with this that Miss H. Mews, of the University of the Witwatersrand, in a paper at the International Conference on Scientific Information last November, argued that it is a first responsibility of any central government to set up a central scientific and technical library and a national scientific and technical information service, either as an independent entity or attached to some existing institution. This has already been recognized as a primary need by the United Nations Educational, Scientific and Cultural Organization, which assisted, for example, the organization of the scientific documentation centre, Insdoc, in India. In the Union of South Africa, the Library and Information Division of the Council for Scientific and Industrial Research was from the start planned on broader lines than as a library service to the Council's laboratories only, while the Federation of Central Africa is at present considering grafting a similar service on to the library of the University College of Rhodesia or one of the existing scientific research institutes.

To a certain extent, the Department of Scientific and Industrial Research, which has been made responsible for the new National Lending Library for Science and Technology, now being planned at Thorp Arch, Boston Spa, Yorks, has, since a recommendation to that effect was endorsed by the Advisory Council on Scientific Policy some five years ago, been developing its Information Division to help inquirers over the whole field of science, apart from the military sphere. In an address on the work of the Department which he delivered to the Society of Chemical Industry at Exeter last year, Sir Harry Melville laid some stress on this function of the Department which, he said, it is proposed to extend further. In view of the success of the Department's regional offices in Edinburgh and in Wales, it was thought desirable to extend the facility over Great Britain; for although the staffs in these offices could not be experts on everything, they could provide the links whereby information could be obtained very quickly. Dr. W. L. Francis stated on September 24 that further centres already exist at Manchester, Birmingham and Newcastle upon Tyne, and others are being planned where possible in co-operation with other libraries, universities, technical colleges, chambers of commerce, etc.

There would appear to be some danger here of overlapping with the work of the Association of Special Libraries and Information Bureaux, which for more than thirty years has been functioning effectively in precisely this field; but apart from this, the success of the development will depend largely on the calibre of the regional officers. Sir Harry Melville's address, however, added little to the very meagre accounts of the work of the Intelligence Division of the Department which have hitherto appeared in the Department's annual reports; some comprehensive survey of its activities and its resources for that work appears to be overdue, particularly in view of concern currently entertained as to the ability of the Council of Scientific and Industrial Research to secure adequate resources for its work as a whole. That the position is, however, improving is indicated by a written answer in the House of Commons on March 25, when Mr. H. Nicholls, Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, stated that provision has been made in the five-year plan for 1959–64 of the Department of Scientific and Industrial Research for the National Lending Library for Science and Technology to be fully operational in 1962. It is anticipated, he said, that some buildings of the former Royal Ordnance Factory, Thorp Arch, which are being adapted for use by the library, will be ready for occupation by March 1961. When the library is fully operational, it is estimated that the annual cost will be £280,000, and the estimated cost of adapting and equipping the buildings for the library is £250,000.

It is now clear that the new Lending Library is to be independent of the Science Museum Library, although it will take over some of the literature held by the latter, which in future will concentrate on meeting the growing needs of the Imperial College of Science and Technology, London. Apart from the additional cost to the new library involved in this decision, it does not appear that attention has been given to the possibilities of savings both in the purchase of stock and in storage which would follow from the planning of a lending library in some relation to a reference library. For a library which it is intended should function primarily for postal loans, there may be no inherent need to stock its holdings of periodicals other than as microcards, at least if the original periodicals are readily obtainable from the reference collection for photocopying. It appears, moreover, from the location now announced, that the idea that the new lending library should also serve industrial areas of the north of England and the Midlands as a scientific reference library has been abandoned. Dr. D. J. Urquhardt expressed the opinion at Washington that perhaps 75 per cent of the current serials in the Science Library are so little used that one loan copy in the United Kingdom would meet the needs of all users. His statement that about 1,250 serials are sufficient to meet 80 per cent of the demand, if confirmed, has a vital bearing on the economics of regional development and the inter-library lending and stocking that are involved.

There is yet another important aspect to which neither Sir Harry Melville nor the Advisory Council on Scientific Policy refers, and that is the relation of these schemes to the British Museum Library. According to the last report of the Advisory Council on Scientific Policy, the idea of a Science Centre has now been definitely abandoned; but it should be remembered that part of that original scheme involved making the British Museum Library the repository for literature more than fifty years old. No statement has yet been made as to the scope of the new Science Reference Library, but Dr. Urquhardt has indicated that the new Lending Library will only be comprehensive from 1950 onwards. There is a possible gap here to be considered if the national library service is to be as vital and positive as Mr. F. C. Francis recommended in his presidential address to the annual conference of the Association of Special Libraries and Information Bureaux at Nottingham last September.

Mr. Francis said he hopes that in the next four years it will be possible to lay the foundations of a new library service which will give the British Museum the place in the modern world which it occupied at the end of the nineteenth and the beginning of this century. Much that he said in this address is highly pertinent to the development of national library services primarily intended to serve science and technology. He recognized, for example, the inevitability of some decentralization, but he was forthright as to the danger of being conservative and parsimonious in our thinking about libraries. That is what is most likely to prevent their full and aggressive use, and depreciate a real national asset. Mr. Francis believes that the staff of the British Museum Library are able to play a full part in co-ordinating library activities, provided there is an appropriate breakdown of services and sufficient awareness of what was being done in other libraries. He made the pertinent point that special librarians owe it to their clients to be familiar with the resources of the great collections, and ready to take the trouble to find the relevant material.

Reiterating the importance both of adequate financial resources and of seeing that money is not wasted, Mr. Francis remarked again that, with the present growth of literature and the present demands made on libraries, no library can look upon itself as being self-sufficient. It is in this context that it is essential to keep to the minimum the number of institutions receiving in full, for example, government publications, with the considerable cataloguing and storage problems involved. Again, the National Library is the only library with an obligation to maintain and preserve its collections, and this responsibility would be difficult or impossible to distribute. Likewise, it is often the only institution in a country which can provide detailed information on the thousand and one subjects for which no specialized library exists.

The Intelligence Division of the Department of Scientific and Industrial Research thus must take full cognizance of the scope of the British Museum Library if it is to perform efficiently the functions now entrusted to it; and that will be even more the case as its responsibilities for providing scientific advice for our embassies through scientific attachés increase. Sir Harry Melville and Dr. W. L. Francis referred specifically to this function, and the importance of the scientific attaché was also emphasized by Miss Mews, who referred to the value of the two-way flow of information and co-operation which is promoted by the system of scientific attachés and scientific liaison officers. Miss Mews mentioned particularly its bearing on the co-operation of professional and scientific societies, and the potentialities of their co-operation in a national library service appear to have been ignored almost completely in the official approach to the new schemes.

The original Science Centre scheme was designed to facilitate the co-operation of such bodies, with full recognition that their participation offered substantial advantages in economy, both of storage and holdings and in operating costs. It is unlikely in view of the decisions which some of the scientific societies have already been forced to take in regard to library and other accommodation that any Government scheme could to-day obtain the full advantages of co-operation that were possible ten years or more ago; none the less, even informal co-operation could offer very real benefits. This was fully realized by President Eisenhower's Science Advisory Committee, and when that Committee's Panel on Scientific Information reported last December, stress was laid on the value of the contribution to the dissemination of scientific information generally made by scientists and technologists in addition to their regular scientific or technical work. Accordingly, the scheme proposed by the Panel is intended to enable the National Science Foundation to take full advantage of all such initiative, whether informally or formally, and to create no more than the minimum of formal organization. What that minimum is cannot be determined either for the United Kingdom or for the United States without a clear view of the whole field and the potential contribution which a wide range of institutions and professional bodies could make—and this appears to be notably lacking in Britain. Moreover, the responsibilities of the National Science Foundation in regard to science information, which, besides research, includes the support of scientific publications, put it in a much stronger position to influence development and provide missing services than any existing institution in Britain could yet hope to do.

What is most discouraging is the absence of any realization at high level of the importance of an adequate national library service or appreciation of the basis on which it must be built. The Committee appointed by the Minister of Education in September 1957 under the chairmanship of Sir Sydney Roberts was concerned with the structure of the public library service in England and Wales and was charged with advising what changes, if any, should be made in administrative arrangements, having regard to the relation of public libraries to other libraries. It might have been expected, therefore, that the Committee would have given some attention to these broader issues, particularly in view of the place which some of the commercial and technical libraries at, for example, Manchester, Sheffield, Liverpool, Leeds and elsewhere have already taken as regional centres. This development, however, which was so well described by Mr. J. P. Lamb four years ago in his book, "Commercial and Technical Libraries", is virtually ignored in the Committee's report*, as are also the earlier report of the Library Association on the post-war development of the university and research libraries of Great Britain, the Association's proposals for the post-war re-organization and development of the public library service and the McColvin report on which the proposals were based. The Committee recognizes, indeed, that co-operation between libraries is essential, and that existing arrangements embrace all public libraries in the country, as well as many university libraries and those of learned societies, scientific and professional organizations and industrial concerns. It is convinced that the regional library systems must be put on a firmer basis and that both the regional bureaux and the National Central Library should be provided with sufficient financial resources.

Nevertheless, it rejects the suggestion that the regional systems and the National Central Library should form integral parts of one national system, the cost of which would be met jointly by the central Government and by the local authorities and other sources, the contributions to be assessed by a new national committee on library co-operation. Instead, it would place the responsibility for providing a satisfactory system of library co-operation on the existing eight regional library bureaux, financed by compulsory payments from each library authority. Virtually, the sole positive contribution to more effective library co-operation proposed by the Committee is the recommendation that under a new Public Libraries Act all library authorities should be given specific powers to combine or co-operate with each other and to co-operate with education and other authorities.

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* Ministry of Education. The Structure of the Public Library Service in England and Wales: Report of the Committee appointed by the Minister of Education in September 1957. Pp. iv+57. (Cmnd. 660.) (London: H.M. Stationery Office, 1959.) 3*s*. 6*d*. net.

This would indeed remove existing legal obstacles, and the responsibility for seeing that inter-library co-operation is effective would rest ultimately with the Minister of Education, who should, in the Committee's view, exercise a general oversight of the public library service. This is in keeping with the educational functions of the public library service, but is not enough. The real problems in establishing an adequate national library service which will meet scientific and technical needs, among others, have not been faced ; and the extent to which it is a factor in industrial and scientific efficiency and not merely in education is not understood. The contribution which the commercial or technical library of a large local authority could make in developing an economic service is ignored, as are the financial implications which arise when such a body is asked to meet national needs from local resources. If the nation's growing needs for scientific and technical information, educationally or in research, in industry and in commerce, are to be met at any reasonable and practicable cost, full and effective account must be taken of all existing resources, and the means provided for efficient co-operation without making demands liable to impair the efficient discharge of any institution's primary responsibilities. Further, we must proceed boldly and imaginatively to fill lacunæ in the existing structure from national resources, making full use of all appropriate advances in the handling and processing of scientific and technical or other information.

MORE PROTEIN CHEMISTRY

Advances in Protein Chemistry, Vol. 12

Edited by C. B. Anfinsen, Jr., M. L. Anson, Kenneth Bailey and John T. Edsall. Pp. x+687. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1957.) 14 dollars.

THIS addition to the well-known series on "Advances" contains seven articles, each written by masters well versed in the difficult art of weaving together several hundred disconnected papers into a readable whole. The activation of the zymogens, reviewed by Neurath, and the conversion of fibrinogen to fibrin, reviewed by Scheraga and Laskowski, are chemically related phenomena. Each involves the activation of a precursor by the hydrolytic action of a specific enzyme. It is only in the conversion of trypsinogen to trypsin, however, that the process has been fully elucidated, while the activation of chymotrypsinogen, procarboxylase, pepsinogen and fibrinogen each consists of a different and complex proteolysis as yet only partly understood. In fibrinogen, moreover, the splitting by thrombin is followed by a polymerization, the intricacies of which challenge the physical chemist. The discussion of these phenomena becomes highly technical, but both articles contain lucid summaries for the non-specialist.

Literature on the chemical nature of antibodies is a jungle of confusing observations through which Isliker guides us with skill. Their purification, and the complexities of even the simplest immune reaction by whole animals, baffle the biochemist. Decisive advances probably await the production of antibodies by homogeneous cultures of specific cells or, even better, by microsomal particles extracted from them.

Li's short article reviews the structure and biological activity of the melanocyte-stimulating hormones, including the most recent results by himself and Harris on the relations between these hormones and adrenocorticotrophic hormone. Work on prolactin, an interesting protein of molecular weight 24,000 with a cystine bridge screening the terminal carboxyl group, is also described.

The abnormal hæmoglobins are a new field to which Itano has made outstanding contributions; his paper gives a lucid summary of the observations and a thoughtful discussion of the physiological, chemical and genetic problems they raise. I should have thought it an understatement, though, to describe Ingram's work on the chemical differences between normal and abnormal hæmoglobins as a "significant advance".

"Protein Crystallography without Tears" might be the title of Kendrew and Crick's article, a popular exposition spiced with pictures of mermaids and quotations from "Alice in Wonderland". However, the frivolous tone conceals scientific rigour in an introduction to crystallography for the non-physicist. This is followed by a balanced account of X-ray work on fibrous and globular proteins, the latter now fortunately rendered obsolete by Kendrew's three-dimensional Fourier analysis of myoglobin.

Goodman and Kenner's monograph on peptide synthesis describes the newer synthetic methods, followed by more than a hundred pages of tables with data and references for all the peptides ever made.

The book is a mine of useful information and should be on the shelf of every biochemical department.

M. F. PERUTZ

TEXT-BOOKS OF ZOOLOGY

Borradaile's Manual of Elementary Zoology

Thirteenth edition, revised by W. B. Yapp. Pp. viii+769. (London: Oxford University Press, 1958.) 30*s*. net.

General Zoology

By Mary J. Guthrie and Prof. John M. Anderson. Pp. xv+708. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1957.) 60*s*. net.

General Zoology

By Claude A. Villee, Warren F. Walker, Jr., and Frederick E. Smith. Pp. xix+877. (Philadelphia and London: W. B. Saunders Company, 1958.) 52*s*. 6*d*.

THE authors of these books set out to provide a text for a first course in zoology. "Borradaile's Manual" is the thirteenth edition of a standard work which many generations of students found well written and intelligible, and this last revision, coming so soon after the major one in 1955, was in response to criticism concerning illustrations, misprints and errors which then appeared. Guthrie and Anderson's "General Zoology" is planned to replace a standard American work—Curtis and Guthrie's "Textbook of Zoology"—but in preference to a fifth edition an essentially new book has been written which preserves characters of the old, brings the text up to date and introduces an insight into modern trends of zoology. As in Villee, Walker and Smith's "General Zoology", the authors set out to give a comprehensive understanding of the subject, recognizing that anatomy is a prerequisite to an appreciation of the functioning of organisms.

The last two books deal initially with cell physiology, metabolism and reproduction and give the necessary chemical and physical background. A survey of the invertebrates follows and some comparative anatomy of vertebrates (which receives a broader treatment in the work by Villee, Walker and Smith), and there are sections on ecology, evolution and genetics. This wide approach to the subject, which reflects its shifting emphasis, necessitates the pruning of some detailed morphology, and one wonders whether such groups as Rotifera, Acanthocephala, Bryozoa and Hemichordata are included for any reason other than reference. The sections on embryology are concise, but it would be helpful to have a precise account of the movements of presumptive areas during gastrulation. Many illustrations in these volumes are new, especially prepared for the text, and others adopted from elsewhere are redrawn. All are labelled so that uniformity is maintained. The drawings in Guthrie and Anderson are executed with great care; in Villee, Walker and Smith more diagrammatic representations are favoured, and this is in conformity with differences in the text and the more leisurely style in Guthrie and Anderson. There are excellent photographs of living animals.

It is a pity that "Borradaile's Manual" still impresses one with its traditional lack of functional treatment, but this would perhaps demand alterations greater than the publishers would welcome in the light of the book's undoubted popularity and its present low price. The introductory chapter on animal organization could profitably be expanded to reflect recent advances. The detailed morphology, an essential constituent of the type system (in which the reviewer firmly believes), gives guidance in practical work (though scarcely replaces a practical text), but needs supplementary comparative studies to give a better understanding especially of vertebrate evolution. A large number of illustrations (forty-three) have been replaced, and more replacements are promised. Figures have been compiled from a variety of sources, and unfortunately this is reflected in their labelling, which has not been altered and results in an incongruity of style and information which is distracting to the beginner. V. Fretter

NATURALLY OCCURRING QUINONES

Naturally Occurring Quinones

By Dr. R. H. Thomson. (Organic Chemistry Monographs.) Pp. vii+302. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1957.) 50s.; 9 dollars.

THIS interesting class of natural products claimed the attention of organic chemists at an early date on account of the importance of some of its members as dyestuffs; and interest in them has continued ever since and has greatly increased in recent years. They vary in complexity from simple derivatives of benzoquinone through the numerous naphthaquinones and anthraquinones to polycyclic molecules like erythroaphin and hypericin.

In this excellent monograph Dr. Thomson has given a critical account of the chemical investigation of all the natural products that have been isolated, characterized, and identified with fair probability as quinones. He has wisely included a number of compounds that are not in fact quinones, such as the sennosides, barbaloin, and rugulosin, the chemistry of which is so bound up with that of related quinones that their omission would have been rather artificial; on the other hand, he has omitted compounds such as methylene-quinones and phenoxazones which contain quinonoid systems that are not terminated at both ends by carbonyl groups. The great volume of degradative work published on some members of the group is concisely summarized, and the more interesting points in their chemistry, such as the unexpected cyclizations and molecular rearrangements that often puzzled early workers in this field, are fully discussed in the light of more modern results and ideas. The degradations and syntheses described are made easy to follow by the generous provision of structural formulæ. Special care has been bestowed on the listing and nomenclature of the animal and vegetable sources, for which there are separate indexes in addition to the main index. There is an extensive bibliography appended to each chapter with references ranging in age from the Old Testament up to as late as 1957, and there are interesting sidelights on the history and uses of many quinonoid pigments.

This volume is indispensable as a reference book for anyone interested in natural colouring matters, and the reviewer also found it a pleasure to read.

R. I. T. Cromartie

AVIATION MEDICINE

Aviation Medicine

Selected Reviews. Edited by Clayton S. White, W. Randolph Lovelace II, and Frederic G. Hirsch. (AGARDograph No. 25.) Pp. vii+305. (London and New York: Pergamon Press, 1958. Published for and on behalf of Advisory Group for Aeronautical Research and Development, North Atlantic Treaty Organization.) 70s. net.

THESE reviews summarize some recent developments in analytical techniques and instrumentation of use to research workers in the highly specialized fields embraced by aviation medicine.

The relation of some of the material to aviation medicine is tenuous. A. E. Reif contributes a lengthy chapter on the physical properties of aerosols, some of which is out of place in a book such as this. Similarly, T. L. Chifelle's chapter on technical developments in pathology is not wholly relevant, making no mention of aviation medicine: nor does Chifelle mention the promising field of aviation pathology.

I. G. Bowen contributes a useful review of techniques for the measurement of atmospheric ozone and outlines a programme for determining whether or not ozone is a hazard. M. A. Palmer summarizes recent developments in high-speed photography, but fails to give an adequate explanation of image fixation on continuous film cameras. J. Clark contributes a short chapter on pressure transducers and Frederic Hirsch has written a useful review of temperature-measuring techniques. Hirsch omits any reference to radiometry, which perhaps deserves mention, and is mistaken in suggesting that thermocouples can be used to measure absolute zero. B. B. Longwell reviews methods for investigating some of the biochemical and physiological changes which occur during stress.

The remaining chapters are devoted to respiratory physiology.

U.P. Luft surveys the important features of various techniques used in direct spirometry and residual volume determination, but omits bronchospirometry and the measurement of maximum breathing capacity and timed vital capacity.

Clayton S. White has written a comprehensive review which describes the physical methods that have been developed for the analysis of respiratory gases. The paper covers methods based upon the measurement of thermal conductivity, paramagnetism, refractive index, velocity of sound, and absorption, mass and emission spectra. It is in the field of emission spectra that the author has made a significant contribution to this aspect of respiratory gas analysis. This section also contains an extremely useful collection of references. It suffers, however, in that it is not sufficiently critical and an investigator new to the field receives little guidance as to which is the best method to employ in given circumstances.

In a further paper written in collaboration with W. R. Lovelace II, White discusses in detail the use of the nitrogen meter. This section is full of intensely practical details with regard to the calibration, accuracy and use of this instrument. In the opinion of the reviewer it should be read by anyone who proposes to use this important tool of the respiratory physiologist.

The final paper, by N. P. V. Lundgren, presents a comparison of the Rahn-Otis sampler with a method for obtaining end-tidal air from the oropharynx. He does not consider, however, the generally accepted limitation of end-tidal air sampling as a method of determining the composition of the alveolar air during quiet breathing, when the volume of alveolar air is inadequate to wash out the respiratory dead space.

All the reviews in this book are by American authors. Most of the material is of great value to the specialist in aviation medicine. Some of the material, excellent in itself, would have more impact in a different publication.

BIOLOGICAL INFORMATION: THEORY AND PRACTICE

The Biological Replication of Macromolecules

Edited by F. K. Sanders. (Symposia of the Society for Experimental Biology, No. 12.) Pp. vi+255. (Cambridge: At the University Press, 1958. Published for the Company of Biologists on behalf of the Society for Experimental Biology.) 50*s*. net.

At the present moment considerable interest is centred around the mechanisms involved in the transfer of intelligence in biological systems, particularly with respect to the relationship which is believed to exist between the structure of two types of large molecules found in all living organisms, namely the proteins, which were originally regarded as the fundamental molecules, and the nucleic acids, which are now thought by many to be the repository of all the information required by an organism. Unfortunately, although this relationship is probably one of the most important in biology, experimental evidence for it is somewhat slight and may even be conflicting. Thus, for example, several enzyme systems are now known which will produce reasonable facsimiles both of ribonucleic acid and deoxyribonucleic acid from simple substrates, but there does not appear to be any necessity for a specific coding system for this synthesis, nor do the nucleic acids produced appear to have any particular information content built in. Indeed, such systems will willingly accept substrates which they do not normally encounter, and incorporate them into the polymers.

So far as the proteins are concerned the situation is rather different, because *in vitro* systems do not accomplish much more than incorporate radioactivity from individual labelled amino-acids into material of large molecular size, and they appear to be rather restricted in their synthetic capabilities.

However, in spite of the general paucity of experimental evidence, there is a great deal of effort now being expended in attempts to elucidate the type of code which could relate the structures of proteins to those of the nucleic acids, using methods of the kind employed in cryptographic analysis. Apart from the fact that new constituents of nucleic acids are now being discovered at regular intervals, and that work on small polypeptides has shown the existence of structures so far undetected in proteins, the problem is complicated further by lack of information about polynucleotide sequences, and by the fact that the proteins themselves are coded by a complex transposition code, which relates their catalytic surface structures to the residue sequences in their polypeptide chains. Consequently, it is necesary when engaging in this entertaining pastime to simplify the problems to such an extent as to render the conclusions doubtfully significant.

It was probably with intent to discuss the present implications of this type of work that the Society for Experimental Biology decided to organize a symposium on "The Biological Replication of Macromolecules" which has since appeared in book form. The precise meaning of the rather indefinite term macromolecule seems to have eluded the organizers, and the various contributors interpret it as meaning anything from a small polynucleotide to a nucleus, with a few proteins and polysaccharides thrown in for good measure. The general tendency of the contributors has, however, been to discuss the more complex types of structure, with the result that the emphasis is largely on genetical rather than on biochemical phenomena. Outstanding among these papers is an account of the conjugation process in *Escherichia coli K*12, while other papers discuss hereditary mechanisms of bacteria, and phenomena occurring on tumour tissue transplantation and during virus replication.

On the simpler level, there are accounts of remarkably successful attempts to isolate individual nucleic acids by ion exchange, and several papers on protein synthesis including an authoritative exposition of the rules of 'coding'. The general impression given by these papers is that a lot of experimental work is still necessary before the results can be interpreted.

It need scarcely be said that all the articles are of a high standard, and it is regrettable that a volume containing such a wealth of information should not contain an index. Roy Markham

MUSICAL ACOUSTICS

A MEETING of the Acoustics Group of the Physical Society, under the chairmanship of Mr. T. Somerville, was held at the Royal Academy of Music on February 26 to discuss : "Of what Use is Acoustics to the Musician ?". Prof. E. G. Richardson opened the proceedings by introducing a list of possible uses of acoustic knowledge and apparatus, as follows.

To obtain an accurate tuning note. This is an obvious use for an electronic oscillator, amplifier and loud-speaker. The conventional instruments for giving the key-note (in singing) or *A* (in playing) are the tuning-fork or the pitch-pipe or the note given by a wind instrument, usually the oboe in the orchestra. The last two suffer from temperature uncertainties, though there is some advantage in having the oboe giving the *A* since the pitch reached by the player after warming up, even if not precisely 440 vibrations per second, will be one to which all the wind players can conform.

To check the pitch of a recorded performance and of the correct intonation of the different parts in concerted music. This is an interesting pastime which tells one quite a lot, perhaps too much. By its means it is possible to check the intonation and pitch discrimination of a solo instrumentalist or singer during a performance. It also brings out quite prodigious feats of tuning and re-orientation of pitch on the part of a good orchestra. Thus, as was shown by an analysis made of a Dutch tape-recording, at a certain performance of Beethoven's first pianoforte concerto the piano was at 440, to which the orchestra tuned within 1 c./s. When accompanying the soloist the orchestra accommodated itself to his pitch, but rose 2 c./s. higher in the *tutti*. On the other hand, a rather regrettable state of affairs was disclosed in a broadcast of Bach's oboe concerto. Oboe and orchestra tuned to 440, but when the piano came in it was at 435. It says much for the string players that they overcame this handicap by playing at 439 (to which the oboe had dropped) when accompanying the solo, and at 435 in the ensembles with piano.

The pitch generally tends to rise above the tuning note during *forte* passages, probably because the notes of the wind instruments tend to rise in pitch with the blowing pressure. The tests also showed—what has been long known—that the human voice at its best is by no means so precise in maintaining constancy of pitch as the mechanical instruments.

The fact is that a musician may be most meticulous about notes being in tune at one instant and will tolerate a considerable degree of mistuning at others. It is natural that he should wish the notes of prominent diatonic chords in a composition to be in tune, but care less about passing notes, which may be elided rapidly, or the little unaccented grace notes which the composer writes as a semi-tone above or below a prominent chord note, probably with no intention that they should be rendered as semi-tones. It is also natural that singers asked to descend a semi-tone and return to the original note, in a type of cadence prominent in the sixteenth century, should make the drop less than a semi-tone in anticipation of rising again. It is a question of accent and speed.

To establish a succession of notes to form musical scales. The construction of a musical scale stretching from one note to the other and the historical evolution of scales seems to me a rather arid and arithmetical subject of study.

Whether our musical sense is an occidental or an oriental one, we all seem to agree that the scale shall cover an octave (though it is true that, in modal counterpoint, the 'stretch' was regarded on occasion as exceeding the octave). Also, rather surprisingly, we all seem to divide the octave of the scale into seven steps whether these are based as in Western music on tones and half tones, or whether, as in Eastern music, some of the intervals are third or quarter tones. In physics, we are mostly Pythagoreans, that is to say, we think of the octave as a length of stretched string which is sub-divided into shorter pieces of string bearing fixed ratios to the whole, but throughout the ages there has existed a type of musicologist who conceives—to me—more complicated sub-divisions, which he advocates as *the* perfect scale.

For most of us two scales suffice, the major and minor of just temperament. Formerly, as is well known, there were six scales in Western music, all having two semi-tone intervals placed at different points in the scale and rejoicing in the lovely names of Dorian, Phrygian, Lydian, Mixolydian, Aeolian, Ionian (thinking in terms of the pianoforte we can say that these had as key-note in turn *D, E, F, G, A* and *C*, but were entirely made up of the white notes). Of these, that based on the note *C* became the major and that on *A* the minor scale. Later, when composers learnt to harmonize, they wanted to make a composition modulate into other keys, and although this was possible for singers and for players on the viols and sackbuts of the epoch, it was not so on a wind instrument with side holes, or on instruments with keyboards, because the frequencies of some notes on the new tonic (key-note) were not equal to any of those of the old key. So a compromise had to be reached, and after various trials the equi-tempered scale, in which the semi-tone is equal to the twelfth root of two, received the support of Bach (who wrote for it his "48 Preludes and Fugues") and became established.

An orchestra or a choir then, accompanied on a keyboard instrument, had to follow equal temperament. Singers, who in common with string players and trombonists have the pitch of the tones they produce variable at will, often claim that when singing unaccompanied (*a capella*) they use the untempered scales. But they are not justified by pitch analyses which have been made using tape records in the way already mentioned. Hard facts show that both they and unaccompanied string quartets use a temperament which is mid-way between the just and the equi-tempered. It is, of course, possible to hear music played on keyboard instruments in just temperament, in a limited number of keys. Such instruments have red and green as well as black and white keys, but require an expert to play on them.

To provide a scientific basis for theories of harmony. It is impossible in a short space of time to give a complete history of the ideas of consonance and dissonance of intervals. It is well known that Helmholtz gave the physicist's and physiologist's view of the basis of dissonance. To him it was a question of the relative number of beats between two tones sounded together as a chord. The more frequent these, the greater dissonance. He made a graph showing the number of beats for each interval of the major scale. But to a musician these matters are not so simple. In fact, some of the ideas of Helmholtz on this question of discords have since been discredited.

In classical music the striking of a discord is rather like the tasting of wine or of sauce. The ear, like the palate, has to be prepared for it ; it is then savoured and it should be followed by some contrasting sweeter sensation.

This was how it was with discords in the classical period of harmony. At first only the octave and the fifth were regarded as concords. It is supposed that the other intervals evolved in the theory of harmony on the basis of a series of upward jumps of a fifth and downward jumps of a fourth. In this way the major and minor thirds appeared and also the seventh. At first the fourth was regarded as an imperfect interval, but by the fifteenth century the root tone, third and fifth formed the accepted concord. Only when the third above the fifth was added to form the seventh above the root of the chord was a discord felt, and this discord had to be prepared by first appearing in a concord and resolved on the following chord in a special way. Later, other thirds were added above the seventh to give the ninth and the eleventh.

It was Bach who found that the discord could be made more piquant by not preparing it, and since his time a composer has followed his whim in this matter. In turn, the necessity for resolution has ceased to be felt by composers. Wagner did not resolve ninths, and Ravel treated elevenths as consonances.

To me the necessity for resolution and not the counting of beats is the essence of a discord. If I do not feel, for example, the seventh on the fifth note of the scale to lead on naturally to the chord on the key-note or any other concord, that chord is free in its progression and so becomes for me a concord.

To measure the acoustic spectra of musical instruments in order to study and improve functioning. Perhaps this is the most rewarding service which the scientist can perform. There exist firms in the musical instrument trade, perhaps more numerous in the United States and Germany than in Britain, which are well aware of the possibilities of acoustic spectrometers and employ people competent to operate them. Adjustments are then made, for example, in the thickness of the belly of a stringed instrument, in the metal of an organ pipe, so that the 'voicer', or his counterpart outside the organ-building trade, can observe the effect on the formant of the instrument which in turn governs the spectrum and the efficiency of the instrument. Not only are such studies carried out by employees of firms, but physicists who are also music amateurs have spent a lifetime of leisure in such work. One need only refer to what Dr. F. A. Saunders has done for the violin and viola in Massachusetts and Dr. W. Lottermoser for the organ (and certain other instruments) in Eastern Germany.

To make experiments with new spectra (on electronic musical instruments). The advent of the electronic organ has given harmonic innovators a very useful tool to try experiments on, though they do not always realize that the loud-speaker of the instrument can superpose its own formant on the register in which the player elects to play his new-fangled music. This new electronic composing is not very popular in Britain, but there exist flourishing groups of its exponents in Germany, Italy and Switzerland.

To obtain design data on concert halls and music rooms. Perhaps in this matter, the musician especially realizes his debt to the scientist who works in acoustics. Auditorium acoustics must remain largely subjective, and musicians reserve their right to say when a hall is good for the performance of music—the difficulty is that all do not speak with one voice on such topics. Nevertheless, when composers and performers are able to say what they want—in reverberation, relative weight to different parts of the gamut and so forth—the acoustic consultant is usually able to advise the architect so that a concert hall or music room satisfactory to its users results.

Dr. B. W. Robinson, continuing the discussion, said that most musicians got on quite happily without studying acoustics. Also, he thought that not many instrument makers used the precision electronic apparatus now on the market for calibrating their products. Prof. Richardson had, however, omitted to emphasize the importance to a musician of the latest high-fidelity reproducing equipment, which was a great boon to an artiste wishing to judge, after listening to himself, to what extent his performance had improved. Self-recording was also of use in teaching elocution, and for singers to show them how bad their pitch discrimination often is.

Mr. D. M. A. Mercer said that acoustic testing with modern equipment could teach the craftsmen tricks not in the text-books and enabled the organ builder to determine how many stops would be required on an organ design for a new church. By its means, Dr. R. W. Young in America had been able to formulate the best tuning system for a pianoforte. This was never done exactly in accordance with the equi-tempered scale.

Dr. A. E. Brown said that he found a knowledge of acoustics helpful in learning to play a musical instrument, for example, in forming the best embouchure for the French horn.

Mr. A. Rakowski referred to the importance for music of having people trained to take full responsibility, from the artistic point of view, for making musical recordings. In the present state of perfection of sound technique in disk recording, radio and film, it is possible for recorded music to achieve a very high degree of artistic value, but people who work in the technique should have a knowledge of both acoustics and music. In the Music Academies of Warsaw and Detmold, special courses have been established for training such personnel.

Dr. H. D. Parbrook thought that there was too much of the music student's time devoted to theoretical study of scales and tuning. Not enough attention was paid to the tonal qualities of electronic musical instruments.

Mr. Nightingale also emphasized the importance of the tape recorder to the virtuoso to improve his playing.

Dr. H. Lowery recalled Sir Hubert Parry's dictum that the acoustical knowledge of a student varied inversely as his knowledge of music. He thought there still was too big a gap between the teaching of acoustics and the requirements of the musician. He said that an understanding of auditorium acoustics was most important to the composer. It was because Bach had an instinctive knowledge of this that his works were so well adapted to the baroque style of building which was prevalent in his day.

E. G. RICHARDSON

VAN ALLEN RADIATION OF SOLAR ORIGIN

By Prof. PAUL J. KELLOGG
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A NUMBER of authors[1] have proposed that the radiation discovered by Van Allen and co-workers[2] results from the decay of neutrons produced in the Earth's atmosphere by cosmic rays. There is some doubt, however, as to whether the low-energy (< 1 MeV.) radiation near the Earth, which on this hypothesis would be due to the β-decay electrons from thermal neutrons[3], is not too intense to be attributed to this source. Although the albedo source is not yet completely ruled out, one should consider other sources for the Van Allen radiation.

The Van Allen radiation is observed to be divided into two zones, and it has been suggested that the inner zone results from neutron albedo, while the outer zone is due to solar particles. This suggestion may be right, but does not help if the inner zone radiation is too intense to be accounted for on the albedo hypothesis. Nevertheless, streams of solar particles are very likely candidates as sources of Van Allen radiation and it is necessary to consider them in more detail.

The picture of the Van Allen radiation which we shall present is rather similar to that published by Gold[4]. We suppose with Gold that part of the Van Allen radiation has its origin in streams of solar gas which somehow become trapped in the Earth's magnetic field. The mechanism for this trapping is not understood, but it is reasonable that, since the pressure of the Earth's magnetic field varies as r^{-6}, most of the gas is injected at a rather constant distance from the Earth. The particles of the gas diffuse away from their radius of injection, but the mechanism for diffusion which we shall present is different from that suggested by Gold.

It is a well-known result of the perturbation theory of the motion of a particle in a slowly varying magnetic field that the magnetic moment of the particle due to its helical motion is a constant of the motion to a high degree of accuracy. Our diffusion mechanism maintains the constancy of $W_{\perp}/B$, so that particles which diffuse toward the Earth into regions of stronger magnetic field must also acquire energy. We discuss this acceleration in detail below. As the particles diffuse upward and downward they may also be lost to space or into the Earth's atmosphere.

This picture might explain the presence of the two Van Allen zones. With Gold, we assume that injection usually occurs at 5–7 Earth radii. Thereafter, the particles diffuse inward and outward, those going outward being lost in a short time. If the diffusion is very rapid in the region beyond 4 Earth radii and considerably slower in inner regions, then the position of the maximum density will move inward as the diffusion proceeds. We discuss below a possible reason for faster diffusion beyond a few Earth radii. It seems reasonable to suppose that the injected particles have an energy spectrum such that the bulk of the particles have too low an energy to be recorded by the instruments used by Van Allen (~ 15 MeV. threshold for protons) but that some few have sufficient energy. Then we expect that the counting-rate will be high near the Earth, where many of the particles have been accelerated to high energy, and high near the injection point, where there are very many particles, but may be low in between, where many particles have been lost and too few have been accelerated to energies above the detector threshold to make up the deficit. In this picture, of course, the total density of particles in the part of the Van Allen radiation of solar origin continually decreases inward from the region of injection and the dip in counting-rate between the two zones is only an effect of the detector threshold.

In order to illustrate the mechanism for acceleration of the particles in the Van Allen radiation, we consider first the following simple case. Consider a system with a constant electric field in the x-direction and a magnetic field in the z-direction which varies in the y-direction, and consider charged particles moving in the $z = 0$ plane. The constancy of the magnetic moment to high accuracy for this case has been demonstrated by Kruskal[5]. According to the Alfvén perturbation theory[6] of motion of particles the radiation of gyration of which is small compared to the scale of field variation, the electric field causes the particle to drift in the y-direction, with velocity v_y. The gradient in B_z causes the particle to drift in the x-direction with velocity v_x. Here:

$$v_y = -c\frac{E_x}{B_z} \qquad v_x = -\frac{c}{e}\frac{W}{B_z^2}\frac{dB_z}{dy} \tag{1}$$

where W is the energy of the particle. The gradient in the magnetic field, therefore, carries the particles into regions of higher or lower potential, depending on the signs of E_x, B_z and dB_z/dy. Since the total energy is constant, the kinetic energy will be decreased or increased. Rather extreme examples of these orbits are illustrated in Fig. 1.

Now we consider the motion of particles trapped in the field of the Earth. As is well known[4], the particles have a very fast gyration around the lines of force, a somewhat slower back-and-forth motion along the lines of force, and a still slower precession around the Earth due to the gradient of the Earth's field. It is this last motion which is of importance here. Since the Earth's field is somewhat irregular, the gradient will cause the particle to precess faster at some longitudes, slower at others. We consider two sources of electric field. First, during a magnetic storm the changing magnetic field of the Earth will produce electric fields. Secondly, various collective oscillations, in particular flute oscillations, may produce electric fields.

We cannot discuss flute oscillations properly at the present time, because we do not understand them. The criterion given by Longmire and Rosenbluth[7] for flute instability, namely, that the magnetic field confining the plasma be convex outward, cannot

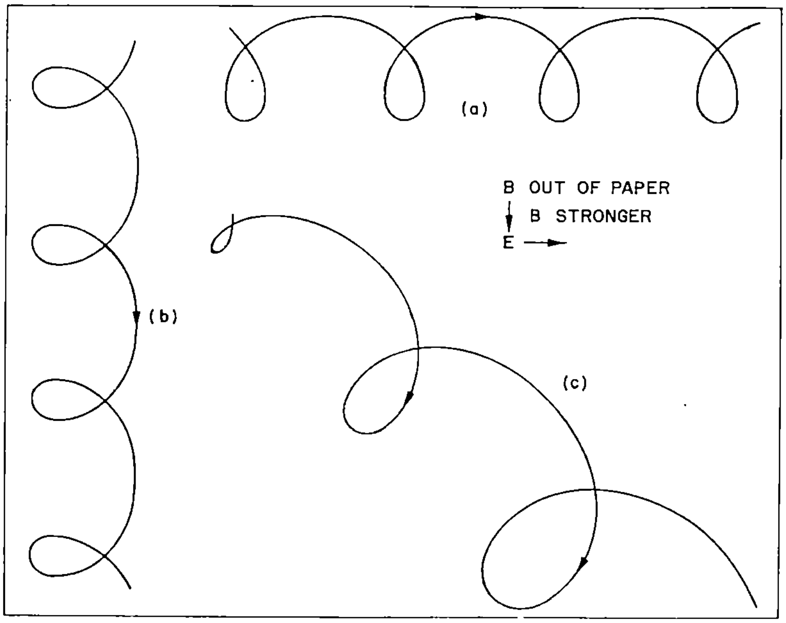

Fig. 1. Typical particle orbits: (*a*) $E = 0$, drift produced by gradient of B; (*b*) $dB/dy = 0$, drift produced by E; (*c*) combined effect of E and dB/dy

be correct, or the Van Allen zone would not be able to trap any radiation; it would be flute-unstable at its upper boundary. It can be shown that neither the conductivity of the background gas, nor 'thermal' dispersion of the particles which would smear out the flute oscillations before they could develop, is sufficient to prevent growth of instabilities at distances less than about 100 Earth radii. Longmire and Rosenbluth neglect the change in energy of the magnetic field, which seems incorrect since the energy of the field is reduced by a quantity of the same order as the plasma energy, and it is probably this neglect which makes their treatment inapplicable in the present case. Intuitively, we might expect that a magnetic field would be rigid enough to confine a very low density of plasma, and that the condition for flute instability should involve the ratio of plasma energy density to field energy density. We may therefore speculate that flute instabilities may be important in the outer parts of the Van Allen radiation, where the field is weak, may account for the approximate r^{-6} decrease of its intensity, and may produce a much faster diffusion in this region.

Both these electric fields have zero time average, so that if the Earth's magnetic field had rotational symmetry they would not produce any net change of particle energy. However, in conjunction with the space-varying gradient of the Earth's field, acceleration and deceleration may be produced. For example, suppose the electric field has a positive value E for a time t and a negative value $-E$ for the same length of time. While the electric field is positive the magnetic field gradient will carry the particle through a potential difference eEv_1t, and while it is negative the particle will be carried through a potential difference $-eEv_2t$, where v_1 and v_2 are average precessional velocities produced by the gradient of the Earth's field at the appropriate longitudes. If $v_1 > v_2$ then the particle will have a net gain in kinetic energy:

$$eE(v_1 - v_2)t \qquad (2)$$

and vice versa. The magnetic moment of the particle, $W_\perp/B$, will be constant, and so if the particle gains energy it will move into regions of stronger field, and thus nearer the Earth, and vice versa. Thus, the electric fields of magnetic storms coupled with the irregularities in the Earth's field will produce a diffusion of particles inward and outward and at the same time an acceleration of those particles which happen to go inward.

The orbits of the particles can be discussed in more detail using, in addition to the constancy of the magnetic moment, the constancy of the integral $J = \int v_{\parallel} dl$ taken between turning points[7]. We present one result only. As the particles diffuse, their turning points move on lines which are roughly radial.

The use of these two constants is the major difference between the present treatment and that of Gold. Gold assumes that irregularities in the field, or electric fields, separately, can produce diffusion. This can only take place if at least one of J and $W_\perp/B$ is not conserved. In a dipole field, the orbit of the particle's guiding centre can be specified by giving three parameters, for example, the energy of the particle, its pitch angle at the equator, and the distance from the Earth at the equator. If in addition to J and $W_\perp/B$ the energy of the particle is constant, as it would be in the case of static magnetic fields of whatever irregularity or of slowly varying electric fields the time average of which is zero, then the particle cannot diffuse but follows a prescribed orbit, the three parameters of which are determined by the three constants of the motion.

Gold's treatment implies that J is not constant. Unfortunately, no estimates exist for the rate of change of J, and so the efficacy of his diffusion mechanism cannot be estimated.

We now make a very rough estimate of the rate of diffusion. Since Van Allen particles do not approach nearer than 1,000 km. to the Earth, they will not be affected by irregularities in the Earth's magnetic field of scale much less than 1,000 km. We may expect, then, that the principal irregularity will be that produced by the Earth's octupole moments, which contribute about 10 per cent of the Earth's surface field. The wave-length of the field is one-third of the Earth's circumference, so that particles which precess around the Earth will be most strongly affected by those Fourier (time) components of the electric field which have the same period as the time the particle takes to precess one-third of the distance around the Earth. This time is given by a modification of equation (2):

$$\tau = \frac{1}{3}\,\frac{2\pi R}{\dfrac{c}{e}\,\dfrac{W}{B^2}\,\nabla_\perp B} \approx 10^4 \left(\frac{R_E}{R}\right)\left(\frac{1}{W}\right) \qquad (3)$$

where W is the energy of the particle in MeV. and τ is in seconds.

During magnetic storms the magnetic field-changes have periods of a fraction of a minute to a few hours.

Only particles of energy greater than 1 MeV. are, therefore, able to take advantage of these changes. For particles of lower energy a different approximation must be used. We take $300\gamma = 3 \times 10^{-3}$ gauss as a typical change of the magnetic field in this time and E approximately equal to $R\mathrm{d}B/c\mathrm{d}t$

$$\approx 3\,\frac{R}{c}\,\frac{10^{-3}\text{ gauss}}{\tau}$$

The change in energy during one cycle of the electric field is given by equation (2). Since B varies by 10 per cent at the surface and decreases as $1/R^2$ compared to the dipole part, we may expect $(v_1 - v_2)$ to be of the order of $\frac{v}{10}(R_E/R)^2$ and vt to be one-third of the orbit circumference. During one cycle, then, we estimate:

$$\Delta W = eE\,\frac{vt}{10} = W\left(\frac{R}{B}\frac{\mathrm{d}B}{\mathrm{d}z}\right)\left(\frac{3\times 10^{-4}\text{ gauss}}{B}\right)\left(\frac{R_E}{R}\right)^2 \quad (4)$$

$$\approx W(10^{-3})\,\frac{R}{R_E}$$

Over a long period, T, since this is a diffusion phenomenon, the root-mean-square (r.m.s.) change $\Delta W/W$ will be proportional to $\sqrt{T/\tau}$. Here T is counted only during magnetic storms. We estimate that magnetic storms are going on 0·1 of the time, and so:

$$\frac{\Delta W_{\text{r.m.s.}}}{W} = 10^{-3}\,\frac{R}{R_E}\sqrt{\frac{T}{10\tau}} \quad (5)$$

where T is now total elapsed time. The time (in seconds) for the particle to make a change of a factor of 2 in its energy is of the order of:

$$T_2 = 10^7\left(\frac{R_E}{R}\right)^2 \tau = 10^{11}\left(\frac{R_E}{R}\right)^3\left(\frac{1}{W}\right) \quad (6)$$

with W in MeV.

This estimate is very rough and is certainly not to be trusted to within a factor of 10. As it stands, however, it gives a diffusion time of 10^9 sec. for a 10-MeV. particle at two Earth radii, which is about 1,000 times shorter than the scattering time for protons, and comparable with that for electrons. The estimate is not valid for particles of energy less than 1 MeV., but an appropriate approximation in that case indicates a diffusion time of the order of 10^{11} to 10^{12} sec., which is somewhat longer than the scattering life-time of either protons or electrons. The diffusion is therefore not capable of supplying low-energy particles to the inner Van Allen zone, as they will be scattered down into the Earth's atmosphere before diffusing very far. Of course, low-energy particles of solar origin might still be supplied directly to the inner zone during times of low-latitude auroræ.

In our opinion, the outlook for Gold's diffusion mechanism is similarly pessimistic. The rates of change of the two near constants of the motion, $W_\perp/B$ and J, are probably very rapidly varying functions of the particle momentum, since the asymptotic expansion, for $W_\perp/B$ at least, vanishes to all orders[5]. The intensity of high-energy particles shows that they are trapped for a long time, so diffuse fairly slowly; therefore, the low-energy particles probably diffuse even more slowly than by the mechanism considered here. We are therefore left with neutron albedo, low-latitude-auroral streams and, possibly, high-altitude nuclear explosions, as the possible sources of the low-energy Van Allen radiation in the inner zone.

I wish to thank Prof. T. Gold for helpful discussions concerning both the present article and his own theory of the Van Allen radiation, and also Profs. E. P. Ney and J. R. Winckler.

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A NEW THEORY OF THE SOLAR CORONA

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In the following discussion we will consider the experimental facts which are known about the solar corona and show that these facts are consistent with a model of the corona quite different from that currently accepted.

According to the present model, the solar corona consists of a gas of electrons and protons with a small mixture of heavy elements which is isothermal at a temperature of approximately a million degrees and which is in hydrostatic equilibrium in the gravitational field of the Sun. The alternative model which we propose is that the solar corona consists of trapped charged particles moving in the magnetic fields of the Sun, very like the charged-particle cloud surrounding the Earth which has recently been discovered by Van Allen[1] and his collaborators.

Although hydromagnetic effects in the solar corona have been discussed (see, for example, Alfvén[2]), the idea of the corona as a trapped charged particle assembly has, to our knowledge, not been proposed.

The solar corona is usually said to be very much hotter (10^6 deg.) than the bodies in contact with it (6,000° for the Sun, 100° for the outer boundary). It is not known what supplies its energy, but probably the heating is a hydromagnetic effect produced by the turbulent motion in the outer part of the Sun, or by 'granulation waves', as suggested by Schwarzschild[3]. There is no general agreement as to the details of this heating mechanism, nor as to the particle energy spectrum which it produces. A lower limit to the supply of energy to the corona may be easily set by computing known losses of energy such as radiation in the observable regions and evaporation from the outer corona. Van de Hulst[4] estimates that the whole energy of the corona must be supplied every 10^5 sec. This time is so short that many features of the corona cannot be expected to be in thermal equilibrium. For example, the collision time for an electron at one solar radius above the surface, where the density is 10^6 electrons/cm.^{3}, is of the order of 10^2 sec. for a 100-eV. electron but is about 10^5 sec. for a 3-kV. electron. Therefore, if the heating mechanism accelerates some electrons to energies greater than 3 kV., these electrons may have energy supplied faster than they lose it by collisions. We may expect, therefore, that in small regions of the corona those electrons having energies in the vicinity of 100 eV. have approximately a Maxwellian distribution of energies, but there may very well be a very long tail of high-energy particles on this distribution. Since the time for exchange of energy between heavy ions and electrons is much longer than that for particles of the same mass, we may expect that the electrons may have a different 'temperature' from the ions, where now temperature refers only to the Maxwellian distributed part of the energy spectrum.

It is likely that the corona contains magnetic fields of 1–10 gauss so that a 100-eV. electron has a radius of gyration of about 10 cm. In 10^5 sec. and with a collision time of 100 sec. such electrons diffuse only a negligible distance. We cannot, therefore, expect that the corona is in anything like equilibrium with a distribution given by the Boltzmann factor $\exp(-MG_m/RKT)$.

Deviations from thermal equilibrium are, in fact, required by the observations. The high temperature, or more properly energy content, of the corona is deduced from: (1) the scale height of the corona; (2) ratios between the populations of ionization states of heavy atoms; (3) Doppler broadening of emission lines; (4) measurements of radio intensity; and (5) Doppler broadening of the Fraunhofer lines. All these measurements give different temperatures (except 5, which gives only a lower limit). We can understand this if the different processes are affected to a different degree by the lack of thermal equilibrium.

In the following we will discuss the properties of the corona listed above in terms of their present interpretation together with their explanation in terms of our suggestion. In addition, we will consider certain observational facts about the corona which are ignored in the current interpretation, but which, however, can be understood on the basis of plasma trapped in a solar magnetic field.

Scale Height of the Corona

Observations of the brightness distribution of the corona during eclipses show that this brightness varies approximately as $1/R^6$, where R is the distance from the centre of the Sun. This experimental fact, first discovered in the eclipse of 1898, is sometimes referred to in the literature as Turner's law. This observation is the basis for the determination of electron densities in the corona on the assumption that the visible light is Thomson-scattered by free electrons. A brightness distribution varying as $1/R^6$ implies an electron density which varies as $1/R^5$ because of the geometry of the problem. Fig. 1 shows a plot of the inferred electron coronal densities and a graph of the expected electron densities for an isothermal atmosphere held by the gravitational field. We have also shown in this figure the profile of intensity of the Van Allen radiation, in units of the Earth radius rather than in units of the solar radius as is done for the corona observation. It can be seen that the principal difference between the observed coronal electron densities and the number of particles in the Van Allen radiation is that the Van Allen radiation has a pronounced maximum where the corona electron density apparently does not. At large distances from the trapping object, however, it appears that the decrease in intensity of the Van Allen radiation is very much like the decrease of electron densities in the corona.

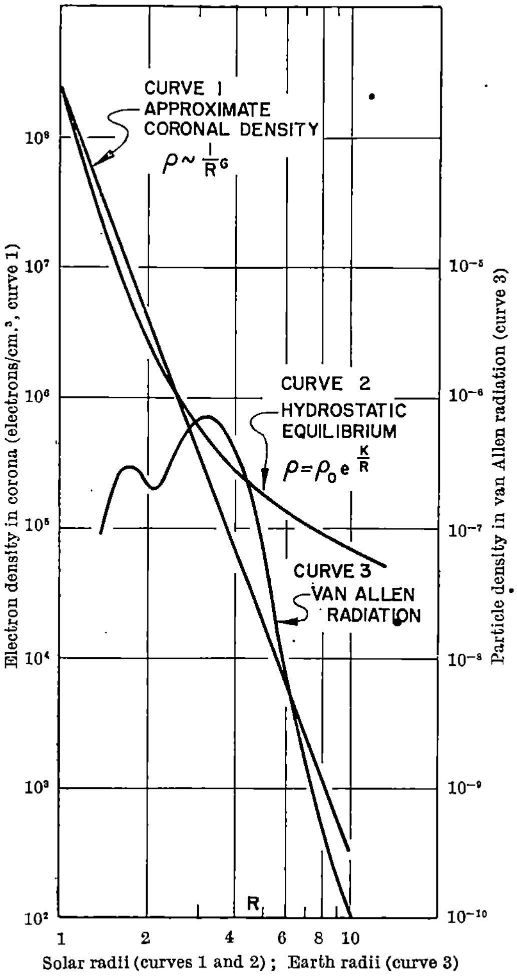

Fig. 1. Plot of electron densities in the corona and Van Allen radiation around the Earth. Curve 1, coronal electron densities vs. radius from the centre of the Sun measured in solar radii; curve 2, an arbitrarily normalized hydrostatic equilibrium curve, such as would apply to the million degree isothermal corona; curve 3 (scale at right), inferred particle densities in the Van Allen radiation (ref. 12) obtained from *Pioneer III* data by multiplying the counting-rates reported by Van Allen and Frank by a factor of 5×10^{-11}. This is equivalent to assuming that the particles measured by them are relativistic particles

Reference to Fig. 1 shows that the particle densities in the solar corona and in the Van Allen belt around the Earth are in approximately the ratio of 10^{12}. If it is assumed that the solar source injects particles which could be trapped in either field, then the flux, because of the inverse square law, would be 10^4 times stronger in the solar belts than in the terrestrial belts. In order to account for the remainder of the factor 10^{12}, one would have to conclude that only 1 in 10^8 of the solar injected particles can be captured at the position of the Earth, that is, the solar trapping field is extremely effective in constraining particles to the immediate solar environment. Because the Van Allen radiation has a maximum and then decreases with increasing distance from the Earth, it is clear that the Van Allen belt is not just an extension of the solar corona, as it could be if Turner's law held to the orbit of the Earth.

Because of the limitations in observing the Sun's corona at large distances from the Sun and because of the *F* corona, it is not possible to distinguish by brightness distribution between a power law decrease of the intensity and the function predicted by hydrostatic equilibrium.

In the hydrostatic model of the corona, Turner's law is the experimental fact, and temperature of a million degrees must follow from the consequent scale height, with a mean molecular weight of 1/2.

The similarity of the intensity distribution at large distances of the corona and Van Allen radiation, however, suggest that the same mechanism may be responsible for both. In a crude way, one can, in fact, justify a power law distribution of intensity of the kind indicated by Turner's law. If the trapping of the high-energy particles were produced primarily by a field with dipole components at large radii, this field would be $B = C/R^3$. Since the energy density of the magnetic field is $B^2/8\pi$, the energy density in the magnetic field can be seen to vary as the inverse sixth power of the distance from the centre of the Sun. In magneto-hydrodynamic models one usually assumes that the energy density of the contained particles is some fraction of the energy density of the field. If this were so, and the energy spectrum were unchanging with distance, the number of particles per unit volume would be expected to go as $1/R^6$. It seems quite clear from observations that the Sun's magnetic field is not a simple dipole field, but the possibility of interpreting Turner's law in a theoretical way as indicated above suggests that magnetic trapping in a more complicated field than a dipole field may be the explanation of corona atmosphere.

Ratios between the Population of the Ionization States of Heavy Atoms

Following the discovery by Edlèn that emission lines of highly ionized atoms were present in the spectrum of the corona, the presence of these emission lines was taken as confirmation of a high kinetic temperature. If these emission lines do, indeed, represent the effect of kinetic theory collisions they also imply an extremely constant temperature throughout the solar corona. For example, the ratio of the intensity of the line due to Fe XIV to that due to the line of Fe X should vary by a factor of about 10^5 for a change in temperature of a factor of 2. It is observed that the ratio of the intensities of these lines varies very little with the solar cycle and with position in the corona.

The hydrostatic model takes this to indicate that the temperature of the corona is extremely constant. On our model the constancy of the ratio of these line intensities would arise because the ionization degree depends on the cross-section for ionization by fast electrons in the high-energy tail. Since the atoms would then be ionized by electron impact by an approximately uniform energy spectrum of particles, one would not expect large variations in the intensity ratio of these lines. It should perhaps be pointed out that the ions themselves would be trapped in the magnetic fields and would therefore not reflect hydrostatic equilibrium of the atmosphere.

Doppler Broadening of Emission Lines

The coronal emission lines are observed to have shapes which are accurately those expected for Doppler broadened lines[5]. The corresponding temperatures, however, range from one to four million degrees, so are both higher and more variable than those derived from (3), yet the same atoms give rise to both effects. On our model, the emission lines would give the 'temperature' of the Maxwellian distributed part of the heavy ion energy spectrum. We suppose there are too few ions in the high-energy tail to affect the line shape.

Measurements of Radio Intensity

The radio emission of the Sun at various wavelengths is sometimes considered supporting evidence for the high coronal temperatures assumed in the hydrostatic theory. The apparent temperature which the radio emission indicates for the quiet Sun varies all the way from 10^4 to 10^{10} deg., with the lower measurements actually applying to chromospheric 'temperatures' because of the wave-lengths used. The range of temperature obtained indicates that the phenomena are too complex to understand on a simple isothermal model, but do not contradict our picture.

Doppler Broadening of the Fraunhofer Lines

In the inner corona, Fraunhofer lines are observed with great difficulty or not at all. This is interpreted to be an indication of a very high kinetic temperature of the scattering electrons which leads to Doppler broadening of these lines to such a degree that they can no longer be seen. The Fraunhofer lines appear again in the outer corona, and this is the primary experimental evidence which leads to the introduction, at large distances from the Sun, of an *F* corona or dust corona composed of large slowly moving particles.

The Doppler broadening differs from the other measurements in that it gives only a lower limit to the temperature. The lower limit is somewhat below 10^6 deg. It is also the one effect which is not strongly influenced by the presence of a moderately small fraction of high-energy electrons. Therefore, the 'temperature' of the Maxwellian distributed part of the electron spectrum may be considerably less than 10^6 deg. This is required by our model in order that the Maxwellian distributed electrons do not produce too high a degree of ionization of the heavy ions.

It can be seen from the foregoing that the principal observational facts about the corona can be equally well, if not better, described by our model than by hydrostatic equilibrium in a gravitational field. There are, in addition, at least three outstanding effects, usually ignored in explaining the solar corona, which have a bearing on the suggestion of magnetic trapping. These are : (*A*) polarization of the coronal light ; (*B*) changes of intensity of the corona with the sunspot activity; and (*C*) the infra-red excess in the corona.

(*A*) *The polarization.* The effort to measure the polarization of the solar corona has a very long history dating back to observations in 1851 by Edlund. Considerable effort was made during the 1930's and 1940's to measure the polarization. Prior to these measurements the suggestion was made by Schwarzschild that the Sun's corona was an electron gas and that the light from the corona came from scattering by free electrons. It should therefore have radial polarization in the sense of the magnetic vector in the electromagnetic wave. Because of the attractiveness of this suggestion, most of the polarization measurements assumed radial polarization and consisted of measurements of the intensity with two analysers at 90° to one another. Such a measurement cannot establish the direction of the polarization.

In only four cases, to our knowledge, has the measurement of the polarization been made with three or more analyser angles in order to determine the direction of the polarization. Van de Hulst[4] in his review article ends his discussion with the remark, "Every time that this method has been used, [to measure the direction of polarization] it has suggested deviations from the normal direction. Theoretically, such deviation seems entirely impossible".

Note added in proof: In addition to the measurements quoted, von Klüber[4a] has observed radial polarization in the eclipse of 1952 (sunspot minimum).

One of our purposes here is to review some of the measurements of the direction of polarization and to consider whether such deviations are actually impossible. The probable source of non-radial polarization would be synchrotron radiation from electrons in magnetic fields. The energies required for the electrons are enormously high—higher than one is used to considering. Conversely, if it proves possible to demonstrate the existence of synchrotron radiation, then previous ideas of the solar corona must be considerably revised.

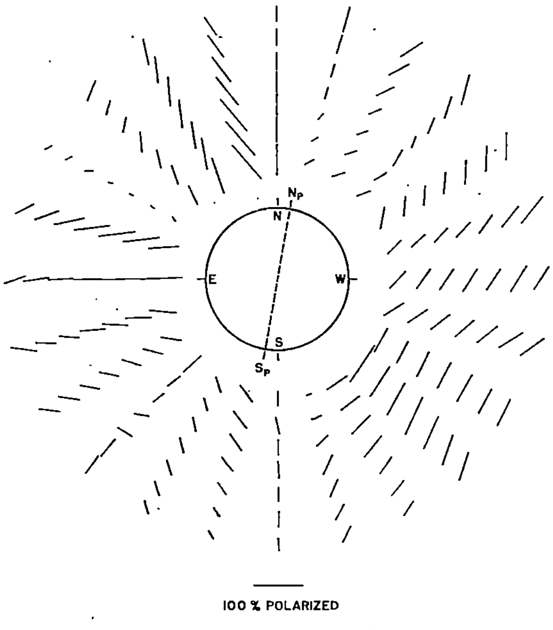

Fig. 2. Plot of magnitudes and directions of the polarization measurements made at short wave-length ($\lambda < 5700$ A.) by Zakharin in the eclipse of June 19, 1936

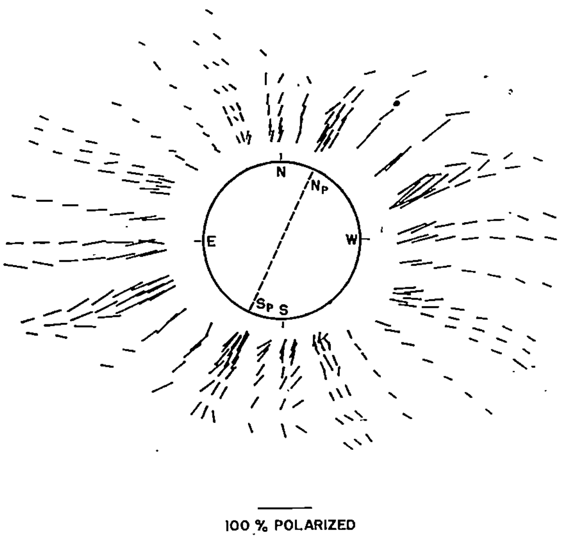

Fig. 3. Plot of the polarization magnitudes and directions obtained by Vashehakidse in the eclipse of September 21, 1941

The first measurement of the direction of the polarization was made by K. G. Zakharin during the eclipse of June 19, 1936[6]. His results are summarized in a table giving magnitudes and directions of polarization in two colours of visible light. These measurements have been plotted in Fig. 2, in which are shown the direction and magnitude of polarization as a function of position around the Sun. If these measurements are, in fact, correct, two remarkable effects are evident. One is the very great deviation from radial polarization, in some directions almost 90°; and the other is the almost complete absence of polarization in other directions. Both these facts could be understood if, in addition to radial polarization due to Thomson-scattering by the trapped particles, there is synchrotron radiation polarized in some other direction. For example, when zero polarization occurred one might assume that the synchrotron radiation gave polarized light perpendicular to the radius vector in approximately equal intensity to that due to Thomson-scattering with a radial polarization. Where the polarization is at almost 90° to the radius vector, one must assume that the overwhelming source of polarized light would be synchrotron radiation. It should be pointed out that high intensity of polarized light due to synchrotron radiation in the visible region requires electrons with kinetic energies of one to ten thousand million electron volts. However, the observations seem to indicate that such polarizations do exist.

The second measurement of polarization with three directions of the analyser was made by Richtmyer during the 1939 eclipse, but unfortunately Prof. Richtmyer died before he could study his plates. These plates are reproduced in various places[7] and have been studied by M. Schmitt[8]. Schmitt measured the polarization along several streamers which were evident in Richtmyer's pictures and found that in the case of one of these streamers the direction of polarization deviated from radial by 30°.

The third measurement of polarization to which we refer was made by Vashehakidse[9] during the eclipse of 1941. The result of plotting these measurements is shown in Fig. 3. It appears here that although there is a lack of radial polarization, the extent of this deviation is not nearly as great as that observed by Zakharin. It should be pointed out, however, that in this eclipse the total light emitted from the corona was only half that observed in the 1939 eclipse, and there may have been fewer particles injected which were capable of producing synchrotron radiation.

The fourth measurement, that of K. Saito, is not available to us.

We believe that very careful measurements of the direction of polarization, especially in the infra-red, would be a crucial test of the presence of synchrotron radiation in the corona. In the infra-red the intensity of the Thomson-scattered light should be reduced and the intensity of the synchrotron radiation increased.

(*B*) *Changes of the corona with the sunspot cycle.* It is well known that the shape and intensity of the solar corona are greatly dependent on the sunspot cycle. At sunspot maximum the corona seems to be almost spherical and approximately twice as bright as the sunspot minimum corona, which is extended in the equatorial plane. Such changes, although difficult to understand in the gravitation equilibrium model, could certainly be explained qualitatively by the injection and acceleration at sunspot maximum of larger numbers of particles in the trapping field. It will be interesting to see whether fluctuations of the solar cycle occur in the Van Allen radiation around the Earth to the same extent that they appear to occur in the solar corona.

(*C*) *Infra-red excess.* A number of authors[10] have measured the ratio of total radiation to visible for the corona and the Sun itself. These measurements are generally in agreement that the coronal emission is rich in infra-red, relative to the Sun.

The explanation of the coronal light as due to Thomson-scattering of sunlight is unable to account for this phenomenon. On the other hand, the presence of synchrotron radiation almost certainly implies that at longer wave-lengths the corona should become brighter. It is worth noting that the infra-red excess in the 1936 eclipse in which Zakharin's polarization measurements were obtained was approximately 4 to 1 relative to the Sun[11]. In other words, the corona had relatively four times more non-visible light than did the solar spectrum. In the corona of the 1941 eclipse, in which smaller deviations from radial polarization were observed, the infra-red excess was also reduced[12].

The strengths of the solar magnetic fields required by our model are determined by the properties of the synchrotron radiation. Unfortunately, the determination of B depends not only on the intensity of synchrotron radiation but also on the energy spectrum of the trapped particles.

If one knew the spectral properties as well as the intensity of the synchrotron radiation one could determine both the energy spectrum of the trapped particles and the strength of the trapping fields. We can, however, make some estimates assuming the following :

(1) The synchrotron radiation is equal in intensity to the Thomson-scattered light in the visible region. This leads to equation 1 :

$$B^2\gamma^2F = 50 \qquad (1)$$

(2) The critical frequency, or frequency of maximum emission, of the synchrotron radiation corresponds to the wave-length of red light. This condition is represented by equation 2 :

$$\gamma^2B = 3\times10^7 \qquad (2)$$

In our equations B is magnetic field in gauss ; γ is the ratio of electron energy to rest mass energy ; and F is the fraction of the electrons which have energy γ mc.^{2}. We have also computed T, the lifetime for energy loss by radiation, and R, the ratio of the energy density of the radiating electrons to $B^2/8\pi$. This latter quantity should not exceed 1. The equations for T and R are :

$$T_{(\text{sec.})} = \frac{5\times10^8}{\gamma B^2} \qquad (3)$$

$$R = 1{,}000\,\frac{F}{B^2}\,\gamma \qquad (4)$$

In Table 1 are the results of these calculations for γ's of 10^2 to 10^4. A γ of 10^2 is ruled out because it leads to an unreasonable value of B ; a γ of 10^4 is ruled out because the energy density is too high for containment in the field. Values of γ near 10^3 lead to reasonable estimates of F, B and R.

Table 1

γ	F	B	T	R
10^2	5×10^{-10}	3,000 gauss	0·5 sec.	5×10^{-12}
10^3	5×10^{-8}	30 gauss	500 sec.	5×10^{-5}
4×10^3	10^{-6}	2 gauss	3×10^4 sec.	0·5
10^4	5×10^{-6}	0·3 gauss	5×10^5 sec.	500

In order to check the hypothesis suggested above, precise measurements of the polarization over a wide spectral range, as well as of the spectral composition of the light, will be important. We are now planning to carry out such measurements during the eclipse of October 2, 1959. In addition to studying the polarization and quality of the spectrum, we hope to be able to determine whether the solar corona has an intensity maximum close to the Sun similar to that observed at larger distances in the Van Allen radiation. Our measurements will be made with a television-type scanning scheme using photomultipliers. The problem of reversal in photographic emulsions has previously masked the possible presence of a maximum. It would seem reasonable that if such a maximum exists it would have to occur close to the Sun, since the injection into the solar trapping field is from the inside, whereas in the case of the Van Allen radiation around the Earth the injection probably takes place from the outside. The basic similarity of the two phenomena, however, suggests, perhaps, that the Van Allen radiation belt could be called the corona of the Earth.

We wish to thank Prof. J. R. Winckler for stimulating and helpful discussions.

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NEWS and VIEWS

Electrical Engineering at Saskatchewan:

Prof. W. E. Lovell

Prof. W. Edward Lovell, who will retire as head of the Department of Electrical Engineering in the University of Saskatchewan, Saskatoon, on June 30, 1960, graduated at the University of Manitoba. He joined the staff of the University of Saskatchewan as a lecturer in 1923, and was appointed professor and head of the Department of Electrical Engineering in 1924. Prof. Lovell has been closely concerned with problems of electric power generation and distribution in the prairie provinces of Canada. He has been widely acclaimed as an outstanding teacher in the field of electric power production, and he has been responsible for introducing many innovations in the undergraduate laboratories.

Prof. Lovell was president of the Association of Professional Engineers of Saskatchewan in 1937, and has been chairman of the Saskatoon Community Planning Commission since 1940. He was a member of the Street Railway Commission in 1932.

Prof. N. F. Moody

Mr. N. F. Moody, head of the Basic Circuit Research Division of the Canadian Defence Research Board, Ottawa, has been appointed professor of electrical engineering in the University of Saskatchewan, Saskatoon, from July 1, 1959.

The Editors regret that, due to difficulties in the printing industry, some sections of this issue of "Nature" have had to be curtailed

During the Second World War, he was at the Telecommunications Research Establishment, Malvern, and, in collaboration with Prof. F. C. Williams, he worked on various aspects of radar research, including automatic range gates, guidance of aircraft by means of radar techniques, and aircraft blind-landing systems. Mr. Moody was head of the Electronics Branch of the National Research Council Atomic Energy Project at Chalk River, Canada, during 1947–51. In 1951 he was appointed superintendent of electronics in the High Explosive Research Establishment of the Ministry of Supply, Fort Halstead, and he was responsible for the elaborate telemetering equipment used in the tests of the first British atomic bomb. Mr. Moody returned to Canada in 1953 and became the first head of the Basic Circuit Research Division at the Defence Research Board, Ottawa.

During the past six years he has established one of the leading laboratories in Canada for the study of semi-conductor devices, and his personal contributions in the field of ultra-high-speed transistor circuits have been notable. Prof. Moody will be associated at Saskatoon with Prof. Arthur Porter, who left the Imperial College of Science and Technology in 1958 to become dean of engineering at the University of Saskatchewan (see *Nature*, 181, 1178; 1958).

Space Research in Britain

In replying to further questions in the House of Commons on April 27 regarding space research, the Minister of Supply, Mr. A. Jones, declined to add to his previous statement (see *Nature*, May 2, p. 1231) and asked members to await the promised statement of policy. Nevertheless, the Parliamentary Secretary to the Ministry of Supply, Mr. W. J. Taylor, welcomed an adjournment debate on this subject on April 29 and outlined briefly what Britain had already done in this field, assuring Mr. de Freitas, who opened the debate, that the Government is giving active consideration to the question of Britain engaging in an Earth satellite programme. British activity in this field began to take shape in the autumn of 1953, when the Royal Society considered the value and practicability of research into the upper atmosphere, extending roughly to about 150 miles from the Earth's surface. In April 1955 five university groups started experimental work and they have since been joined by a sixth. The Royal Aircraft Establishment undertook to develop rocket vehicles suitable for these experiments and, by agreement with the Australian Department of Supply, arrangements were made for the rockets to be launched at Woomera. The first trial flight of the rocket developed for this purpose, *Skylark*, took place early in 1957, and a series of twelve fully instrumented firings began in the spring of 1958.

Mr. Taylor stressed the magnitude of Britain's effort in tracking the Earth satellites launched by the Americans and the Russians and in analysing the data received from them, referring to the international recognition of the very fine work of the Department of Scientific and Industrial Research stations at Slough and Singapore, the Jodrell Bank radio-telescope and of some Ministry of Supply establishments. New information had been obtained about the shape of the Earth and a contribution made to the study of air-drag on satellites and its interpretation in terms of air density. While, however, the Government is considering the possible use of the *Black Knight* research vehicle and the *Blue Streak* ballistic vehicle in an Earth satellite programme, it could not allow any such use to interfere with the place *Blue Streak* took in the military programme of deterrence. It had sought the considered views of the best scientific opinion in Britain, and Mr. Taylor repeated that an announcement as to whether and in what way the United Kingdom should extend its research activities into outer space would be made very shortly. Replying to specific points raised by Mr. de Freitas, Mr. Taylor thought that Mr. de Freitas's estimate of £10 million to £20 million as the cost of a satellite research programme over the next five years might be too modest; further design studies would be needed before reliable estimates could be made. He welcomed, however, the suggestion that the satellites should be designed as laboratories in space, working in a definite scientific field, but he did not think that a satellite programme was so crucially important that the scientific well-being of the country stood or fell by it. He also thought that the dangers of scientific emigration should not be exaggerated, nor the effect on it of any decision regarding space research. There was, and would continue to be, great scope for international co-operation outside the Commonwealth in this field, and Mr. Taylor referred particularly to the International Committee on Space Research, one of the fruits of the International Geophysical Year. It was also expected that an *ad hoc* committee of the United Nations could meet shortly to consider what international action regarding co-operation in the peaceful uses of outer space could profitably be taken at inter-government level.

Manchester Literary and Philosophical Society: New Building

THE foundation stone of the new building of the Manchester Literary and Philosophical Society was laid at 36 George Street—the site of the old building destroyed in an air raid in December 1940—by the Lord Mayor of Manchester, Alderman J. E. Fitzsimmons, on April 30, and it is expected that the new meeting house will be ready in about a year's time. In welcoming the Lord Mayor, the president of the Society, Mr. C. E. Young, said that the building destroyed in 1940 had housed the Society for at least 140 years. Before the building was acquired in 1799 the Society, which was founded in 1781, had met first in the Assembly Coffee House, which was probably in the Exchange Buildings of that day, and later in a room at the back of Cross Street Chapel. Mr. Young referred to the association with the Society of such famous scientists as Percival, Dalton, Joule, Schunck and Roscoe, among its past presidents, and afterwards, in a speech at an informal luncheon, expressed the hope that the Society would become a meeting place of minds from town, university and industry, representing and serving the everyday intellectual life of the city.

Thanking the Lord Mayor on behalf of the Society, Lord James expressed the conviction that there is even more important work for such a Society to do to-day. When it was founded and for the next half-century, an educated man could take all knowledge for his province. That is no longer possible, and one of our greatest needs is to encourage communication between men educated in different fields. Lord James thought the Literary and Philosophical Society could make a very important contribution to the establishment of channels of communication between specialists. By providing a formal and informal meeting place for people with widely differing interests, the Society was preparing to maintain and extend its original task of stimulating the intellectual life of the city. That task would call for the support and encouragement, financial and otherwise, of a considerable body of sympathizers. Mr. Young referred particularly to the need for adequate financial support for operation and maintenance, although the membership of the Society is now 320, the highest in its history. Virtually all the contents of the old centre were destroyed by fire, including the records, the library and Dalton's manuscripts and other relics, and there is a deficit of some £10,000 on the £35,000 which the new building will cost, to be met before the Society can be re-established on a sound financial footing. It is hoped and expected that the lecture rooms will be used by many of the numerous scientific and other societies which are active in Manchester. Both Mr. Young and Lord James paid tribute to the work of the Society's honorary treasurer, Mr. H. Hayhurst, in promoting the scheme.

The Vienna Declaration and Nuclear Disarmament

THE Vienna Declaration, adopted by the participants in the Third Pugwash Conference held at Kitzbuhel, Austria, on September 14–19 and at Vienna on September 20, 1958 (cf. *Nature*, 180, 358; 1957), has been sent, with a questionnaire and a letter signed by Lord Russell, to scientists all over the world to ascertain whether there is general support for the ideas expressed in the Declaration and for further activities based on it. The Declaration affirms that the only restraint against the use of nuclear weapons in war would be agreements not to use them, which were concluded in time of peace: the possession of such weapons is relatively unimportant, as in any future major war each belligerent would feel compelled to undertake immediate production of nuclear weapons, and for a major industrial power less than one year should suffice. The statement recognizes that any agreement on disarmament, and particularly on nuclear disarmament, requires a measure of control to protect every party from possible evasion, and because of the technical difficulties, the need for policies encouraging international trust and reducing mutual apprehension is stressed. The signatories believe that, as scientists, they have an important contribution to make towards establishing trust and co-operation among the nations, and that science can best serve man if it is free from interference by any dogma imposed from outside, and can exercise its right to question all postulates, including its own. The scientific tradition of mutual understanding and of international co-operation can, and should be, extended to many fields of technology.

Quality of Protein Feeding-Stuffs

SIR SOLLY ZUCKERMAN, a member of the Agricultural Research Council and chairman of its Protein Quality Group, writes: The Agricultural Research Council has organized a collaborative investigation into the measurement of the quality of protein feeding-stuffs. Several centres are taking part in a trial designed to establish whether any rapid laboratory tests can give a reliable indication of the feeding value of such materials. Specimens of these materials, some of which have been imported, were kindly supplied by manufacturers who have included, in response to a request to cover as wide a span of quality as possible, samples known to be bad, as well as samples within the commercial range. When it has been completed, the results of the whole trial will be published by the Committees as a whole. In the meantime, however, it is probable that members of the staff of the participating laboratories will be publishing in various journals papers describing work in which some of these samples have been used, but which deal with matters not directly related to the correlations which the joint effort is designed to elucidate. It has been agreed that in any such papers the samples used will be described by the code numbers uniformly used by the whole group.

Australian and New Zealand Association for the Advancement of Science

A REPORT on the future of the Australian and New Zealand Association for the Advancement of Science published in the *Australian Journal of Science* for October 21, 1958, advocates discontinuing the Handbook and Report and making greater use of the *Australian Journal of Science*, which it is proposed to publish monthly. Conferences every year and a half are recommended instead of annually or biennially, but no change in the names or number of the Sections are recommended apart from the formation of a new Section corresponding with the Assembly of Corresponding Societies in the British Association. Stress is laid on keeping the public informed on what science is doing as the primary function of the Association and the report recommends that as much sectional time as possible should be devoted to meetings of the symposium type which present more general matters from several angles.

Journal of Medicinal and Pharmaceutical Chemistry

THIS new journal (1, No. 1, February 1959. Pp. 120. Published bi-monthly; subscription price 115*s.* or 15 dollars per annual volume including postage. New York: Interscience Publishers, Inc.; London: Interscience Publishers, Ltd., 1959) will be mainly of interest to the synthetic chemist engaged in the manufacture of drugs and to pharmaceutical chemists and pharmacologists whose line of research lies in the drug-action relationship. "Chemical-biological correlative work" is defined by the editors as one of the main fields which the new journal wishes to cover. Papers are to be accepted in English, French or German. The increasing number of drugs produced by the chemical industry, all of which need biological evaluation, probably created a need for a special journal to deal with the quantity of work done; the future will show whether this need could not have been covered by the existing journals.

Commonwealth Bursaries Scheme

THE fifth annual report on the Royal Society and Nuffield Foundation Commonwealth Bursaries Scheme covers the year ended December 31, 1958 (pp. 8. London: Royal Society and Nuffield Foundation, 1959), in which 26 bursaries, totalling £13,974, were offered, compared with 18, totalling £8,423, in 1957. Of these 8 were for visits from the United Kingdom, 12 for visits to the United Kingdom and 3 for visits between countries of the Commonwealth other than the United Kingdom; three offers were not accepted. Of the 67 applications considered during the year, 44 were for visits to the United Kingdom, 11 for visits from the United Kingdom and 12 for visits between Commonwealth countries other than the United Kingdom. Most of the applications were of a high standard. Besides the Nuffield Foundation's grant of £5,000, which was received for 5 years from 1959, £2,000 was received through a Parliamentary Grant-in-aid to the Royal Society, £1,200 from Canada, £800 from Australia, £400 from South Africa, £322 10s. from Pakistan, £200 from New Zealand, and £100 each from Ceylon, Rhodesia and Nyasaland.

Studies in Indonesia

THE Jajasan Siswa Lokantara, the local Indonesian foundation for granting fellowships to foreigners studying in the country, is ready to consider suitably qualified applicants in any subject of study. This foundation has considerable funds at its disposal and is independent of government departments; it is prepared to guarantee all reasonable local expenses, including living costs and fares within Indonesia, but owing to the considerable variations in cost of living throughout the territory has refrained from fixing a definite monthly allowance. The intention is to operate a flexible and reasonably generous allowance scheme which will enable Fellows to study where they wish (so far as internal conditions and transport facilities allow), and to establish close relations with Indonesians working in similar fields. Further information can be obtained from the Universities Section, Education Division, British Council, 65 Davies Street, London, W.1.

First All-India Congress of Zoology

THE first All-India Congress of Zoology, sponsored by the Zoological Society of India, which was to have been held last year but was postponed, will be held at Jabalpur during October 24–29, at the invitation of the University of Jabalpur. Further information can be obtained from the General Secretary, Dr. B. S. Chauhan, c/o Zoological Survey of India, 34 Chittaranjan Avenue, Calcutta 12.

Announcements

DR. A. A. MOSS has been appointed deputy keeper of the Department of Mineralogy in the British Museum (Natural History).

PROF. JOHN READ, professor of chemistry in the University of St. Andrews, has been selected for the 1959 Dexter Award which is administered by the Division of History of Chemistry of the American Chemical Society.

DR. H. ALBERT BARKER, professor of microbial biochemistry in the University of California, Berkeley, has been awarded the Neuberg Medal for outstanding work in biochemistry and, in particular, for his discovery of the coenzyme corresponding to vitamin B_{12}. The Neuberg Medal was created to honour Carl Neuberg, a pioneer in biochemistry. It is given annually by the American Society of European Chemists for outstanding contributions in the field of biochemistry.

AN International Congress on Radiology will be held in Munich during July 23–30. Further information can be obtained from the Congress-Sekretariat, Reitmorstrasse 29, Munich 22.

A SYMPOSIUM on Fluorine Chemistry is being arranged under the auspices of the Chemical Society, to be held in the University of Birmingham during July 15–17, covering topics in organic, inorganic and physical chemistry. Further details can be obtained from the Secretary, Fluorine Symposium, Chemistry Department, The University, Edgbaston, Birmingham 15.

THE twenty-first International Congress of Physiological Sciences (Physiology and Pharmacology) will be held in Buenos Aires during August 9–15 under the presidency of Prof. Bernardo A. Houssay. Further information can be obtained from the Secretary, Twenty-first International Congress of Physiological Sciences, Facultad de Ciencias Médicas, Paraguay 2151, Buenos Aires, Argentina.

THE Gordon Research Conferences for 1959 will be held during June 15–September 4 at Colby Junior College, New London, New Hampshire; New Hampton School, New Hampton, New Hampshire; and Kimball Union Academy, Meriden, New Hampshire. The conferences were established to stimulate research in universities, research foundations and industrial laboratories. This purpose is achieved by an informal type of meeting consisting of scheduled lectures and discussion groups. Further information can be obtained from W. George Parks, Director, Department of Chemistry, University of Rhode Island, Kingston, Rhode Island; after June 15 from Colby Junior College, New London, New Hampshire.

INLAND WATERWAYS IN BRITAIN

THE debate in the House of Lords on February 17 on a motion of Lord Ammon's directing attention to the report of the Bowes Committee of Inquiry into Inland Waterways preceded by a few days the publication of the Government proposals in a White Paper (Cmnd. 676). The debate, nevertheless, was welcomed by the Earl of Gosford, who, in replying on the debate for the Government, said that the various suggestions made will receive careful consideration. Lord Gosford pointed out that the main points in the Committee's report were that capital development should continue to be concentrated on the 300 or 400 miles of the more than 2,000 miles of inland waterways in Great Britain which carry busy and remunerative traffic. Another 900 miles carry some commercial traffic but are unremunerative, and the Committee recommends the rehabilitation to navigation of these waterways with the development of other uses and revenue. The remaining waterways have outlived their commercial utility and the Committee proposes a case-by-case review to assess their possibilities and prepare schemes for future treatment.

Lord Gosford indicated that the Government was fully aware of the many interests concerned in these proposals, including water undertakings, drainage and river boards, farmers, anglers, naturalists and amenity, but his reply foreshadowed the Government's proposals in the White Paper. They cover an interim policy over about two years in which some of the Committee's ideas can be tried out experimentally, but while endorsing the Committee's objectives in redevelopment and proposing to set up an Inland Waterways Redevelopment Advisory Committee, and accepting that legislation to facilitate redevelopment is needed, the Government is not prepared at present to commit itself to the detailed procedural machinery suggested. It also considers that the cost of redevelopment should be borne by those who benefit from it.

The Nature Conservancy in its last annual report expressed the view that the findings and recommendations of the Bowes Committee providing for the setting up of a waterways redevelopment board to prepare schemes for redevelopment, but envisaging the participation as new owners of river boards or drainage authorities, water undertakings or local authorities, and, exceptionally, special trusts, are regarded as meeting adequately the Conservancy's needs. Lord Gosford, however, did not refer to the boards, although this question was specifically raised by Lord Latham in the debate. In the White Paper the Government accepts the view that proposals for costly schemes of improvement are not justified in present circumstances and that instead there should be a gradual extension of the work which has already been carried out. The Committee recommended that the Great Yarmouth Port and Haven Commissioners should be reconstituted on a wider basis of membership and with greater powers, and the Nature Conservancy appears to accept this view. Nevertheless, and although the Committee also urged that the demand now for the use and development of the rivers and Broads was greater than ever and their deterioration could be stayed and improvement ensured by a revision in the powers of the Commissioners and a small increase in their income, the Government is not prepared to introduce the recommended legislation without first thoroughly exploring the administrative proposals between the various interests concerned. Discussions between representatives, however, have already begun, including those of the National Parks Commission, although it may be noted that the Committee is not impressed by the arguments for making the Broads a national park.

THE NATIONAL OCEANOGRAPHIC COUNCIL

REPORT FOR 1957–58

THE annual report of the National Oceanographic Council for 1957–58* reviews progress in the two main fields of work of the National Institute of Oceanography: marine physics and marine biology. With a staff of eighty-four (not counting officers and crew of R.R.S. *Discovery II*) and with an annual expenditure of £201,000 mainly met by United Kingdom and Commonwealth Government grants, the effort has been chiefly devoted to studies of the interaction between atmosphere and ocean, water movement on large and small scales, biological fertility of the oceans, and the distribution of marine animals. Basic knowledge of physical and biological processes has also been applied to practical problems.

R.R.S. *Discovery II* spent two periods of nearly three months measuring currents in the Gulf Stream and working stations across the Atlantic in latitudes 48°, 32° and 24° N., as part of the Institute's contribution to the International Geophysical Year. A large part of the fuel was kindly provided by the Woods Hole Oceanographic Institution, and United States oceanographers and vessels collaborated in this international attack on the problems of ocean circulation. Deep-water isohalines, computed from the electrical conductivity of samples taken at a range of depths at stations about 8 miles apart, revealed greater irregularities in water properties and motion than had been inferred from earlier, less-precise observations.

The technique of tracking deep currents by means of neutrally buoyant floats, pioneered at the Institute, has stimulated similar measurements elsewhere, as well as theoretical studies of ocean circulation. Floats have now been made which will send out signals for a few hours each day for a month. The more practical needs of the fisherman and the fisheries scientist for a knowledge of sub-surface currents has also been met by improvements in a simple but ingenious method of recording the orientation and inclination of a container moored in the current. Echo soundings made along 12,000 miles of the ship's track have included detailed surveys of the Porcupine Bank (from which rocks were collected) and large sand waves on the continental shelf to the west of the English Channel which attain 40 ft. in height and 3,000 ft. between crests.

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* Annual Report of the National Oceanographic Council, 1 April, 1957–31 March, 1958. Pp. v+39. (Cambridge: At the University Press, 1958.) 5s. net.

Research on processes operating at the sea surface, in particular wind waves, has been mainly directed at finding a convenient way of measuring the directional distribution of wave energy and to the development of an adequate physical theory relating the wave spectrum to wind, stability, and other factors governing turbulent shear and the exchange of energy between atmosphere and ocean. Theoretical studies of the curvature of random surfaces and the distribution of intervals between 'crests' of random functions enable directional information to be derived from aerial photographs of waves. Other theoretical studies of far-reaching practical significance have been concerned with the estimation of the mean wave energy from the highest waves in a record; with the accuracy of wave measurements using accelerometers in buoys or ships; with the vertical components of motion of a ship heading into sea waves; with the relative merits of empirical formulæ for wave and swell prediction; and with long waves and storm surges. Tidal records initiated by the Institute at Stornoway and Lerwick support the theoretical conclusion that surges arriving from the Atlantic are amplified on passing down the east coast and suggest that large surges are most likely when intense storm depressions travel from the south-west for a long distance along the continental shelf.

The Institute is still the chief protagonist of the wave-interference theory of microseism generation. While there is still need for clarification, it has proved possible to track isolated storms in the North Atlantic by analysis of microseism activity at Kew. There is a practical application in tracking storms and giving warning of heavy swell on coasts facing oceans that have little meteorological cover. An electronic seismograph has been constructed which allows exceptional magnification in the 3–10-sec. range. Other instruments in the course of development include an airborne radar sea-swell recorder and a pressure recorder of high precision which, when used to record waves, can be calibrated by tidal observations.

The Institute's biological work falls into three broad groups: the distribution and taxonomy of marine animals, particularly oceanic plankton, based to a large extent on the *Discovery* collections; the bionomics of whales; and the productivity of oceanic waters. Objects of study last year included: the alcyonarians (revision of the pennatularian genus *Umbellula*); certain families of the isopods (fifteen species, of which five and one family are new); deep-living chaetognaths (including a new species with a method of fertilization hitherto unknown in this group); the distribution and life-cycles of the Antarctic copepod *Calanoides acutus* and of the euphausid *Euphausia triacantha*.

During a spring cruise to the Canary Islands, additions were made to the collection of photographs of oceanic animals, ranging from small planktonic forms to moderately large cephalopods, including a dramatic sequence at 500 m. in which a squid was attacked and eaten by another squid. Observations on the composition and numbers of phytoplankton and zooplankton, compared with those made in the same waters on previous cruises, emphasized the remarkable stability and constancy of the crops in this part of the open ocean in different years. During this and other cruises, particular attention has been paid to the factors controlling rates of assimilation of carbon in regions of dense and sparse phytoplankton, and to the significance of the ratios of chlorophyll *a* and *c* in coastal and oceanic regions.

Largely through the help of whaling inspectors and companies the Institute has been able to examine ear plugs and ovaries from several hundred whales. Ear plug laminations and the corpora albicantia in the ovaries are indices of age and provide valuable evidence on life-histories, rates of ovulation, and on year-to-year changes in the stock. Recovery of whale marks has consolidated and extended earlier inferences about distribution, migrations, and interchange between the south-west Atlantic and south-east Pacific in both directions.

Finally, it is encouraging to record that governmental aid has been increased to allow for expansion of staff, that four investigators from overseas have played a considerable part in the work, and that the effort devoted to the problem of fish detection is welcome evidence of increasing collaboration between the physicists and the biologists.

C. H. MORTIMER

THE ROCKEFELLER FOUNDATION

REPORT FOR 1957

THE annual report of the Rockefeller Foundation for 1957, in which appropriations totalled 42,798,916 dollars, including 8,298,260 dollars for medical education and public health, 5,255,235 dollars for biological and medical research, 5,621,400 dollars for the agricultural programme, 3,570,525 dollars for the social sciences and 5 million dollars to the American University of Beirut, stresses the broadening basis of co-operation among governments, with which the work of the Foundation has brought it into close contact at the local level in every continent. For half a century the Rockefeller boards have been intimately involved in the international community of science and scholarship, particularly in the financial support of scholarship and science abroad, largely through the universities, but using various techniques. Special emphasis is laid on the value of the Foundation's fellowship programme, under which 7,432 men and women from 98 countries, including 1,306 from the United States, have held fellowships for advanced study in 80 countries: of these, 248 received awards in 1957, when 532 persons from 53 countries pursued their training or research in 104 institutions in 20 countries.

Discussing the characteristics of this international community of science and scholarship, the report emphasizes that it is open to all who wish to contribute ideas and its respect is bestowed on the basis of merit, not of authority. Sweeping beyond national frontiers, the community is linked by a strong network of communication through books, scientific and learned periodicals, meetings, and a persuasive flow of travel and personal correspondence, in which much has been done to remove the barrier of language. Development now involves the fullest participation in this community of science and scholarship and it is suggested accordingly that present tensions underline the need to seek out and cherish those elements of modern life which bind men together across national and cultural frontiers. In the United States alone 66,000 persons participated in educational exchange during the year, 52,000 from 145 countries or territories coming to study or teach, and 14,000 Americans visiting 50 countries for similar tasks. Secondly, governments have demonstrated their ability to set political issues aside at selected points to co-operate effectively for the welfare of their peoples, and if international politics has not yet found practicable means for settling disputes, the field of politics could be reduced by steadily broadening the basis of co-operation on the long-range humane interests of man.

The President's review selects for emphasis the Polish science programme on which in May 1957, following a visit of Foundation representatives to Poland, grants of 300,000 dollars for purchase of scientific materials and supplies, books and periodicals and of 175,000 dollars for fellowships for younger Polish scientists to visit other countries were made. The new grants for Poland are concentrated on medical education, public health, the biological and medical sciences and agriculture, as the Ford Foundation, also at the invitation of the Polish Government, has initiated a programme in social sciences and humanities. Of the 25 fellowships awarded, 19 have already commenced study, most in the United States, but 4 in the United Kingdom, and grants-in-aid were also made to 21 more mature Polish scientists.

In referring again to the public health aspects of nuclear energy, the report suggests that the complicated and difficult problems which will accompany massive use of nuclear energy involve special responsibilities for the universities; the Foundation is accordingly supporting several broad programmes of special advanced training. That at the New York University Institute of Industrial Medicine stresses the chemical and radiobiological toxicological problems of the nuclear energy industry, particularly quantitative aspects of environmental contamination; at Harvard and at Pittsburgh problems of air-borne chemical and radiobiological contamination are stressed, while at Johns Hopkins University the primary emphasis is in the expanded Department of Biophysics: each of these institutions is receiving 500,000 dollars.

Dealing with the Foundation's operating programmes, the President reviews in some detail its world-wide study of the virus infections transmitted to men and domestic animals by the bite of arthropods. Under it more than 70 distinct viruses have been discovered, 37 of which have been shown to be members of one or other of three immunologically related families, 27 being located in South America, 24 in the Ethiopian region and 15 in the Oriental region, including India, Malaya, the Indonesian Archipelago, Indo-China and South China. He refers to the rapidity with which, in 1957, following the discovery in India of an agent belonging to the Russian tick-borne complex of viruses, the etiology of the disease and its major epidemiological features were elucidated. This shows the utility of the Rockefeller Foundation's virus programme. A special appropriation of 100,000 dollars will assist the Indian Government with its vaccination campaign and enable Indian scientists to study vaccine production techniques in the United States.

Under the agricultural programme, now in its seventeenth year, the Mexican, Columbian, Chilean and Indian agricultural programmes, the last differing from the others in including direct connexion with a graduate school of agriculture and the correlation of the food crop research projects with the research and training activities of the school, will receive support. The Mexican and Columbian programmes have participated in the National Research Council project for preserving indigenous varieties of corn by systematically collecting samples of every extant variety in the High Andean region, Central America and Mexico, while all three Latin American units are co-operating in the international wheat rust nursery of the United States Department of Agriculture.

THE PLANT BREEDING STATION, NJORO, KENYA

By H. C. THORPE

Department of Agriculture, Kenya

THE new research laboratories of the Plant Breeding Station, Njoro, were opened on August 29, 1958, by the Speaker of the Kenya Legislative Council, Sir Ferdinand Cavendish-Bentinck. He was deputizing for the Minister of Agriculture, the Hon. Michael Blundell, who was unable to be present owing to illness. The ceremony was held in the presence of representatives of agricultural and milling interests, and of a large gathering of farmers from all over the country. After the opening, visitors were shown the field work in progress and conducted through the new laboratories where exhibits had been arranged demonstrating the various problems under investigation.

The building was designed and built by the Ministry of Works, in consultation with the Department of Agriculture, to cater for the special needs of the plant breeding team. The east wing houses the threshing room and cereal-selection laboratory, with space for the storage of sheaf material and packeted seed; special features are the provision of adequate well-lit benching for grain selection, and the arrangement of the layout for ease and efficiency of handling the breeding material. The west wing houses the pathology section, which deals with cereal diseases with special reference to wheat stem rust. The main body of the building consists of the administrative offices, a cereal chemistry laboratory, library, dark room, stores and service rooms, as well as private rooms for individual research officers. Much thought has gone into the planning of the layout, and the architect has designed a light and airy building of pleasing character, yet retaining its strictly functional purpose, for a total cost of £15,000.

The Station is situated at 7,100 ft. in the Kenya Highlands, virtually on the equator, in one of the main wheat-growing areas of the country. It is the headquarters of the Plant Breeding Section, and the main programme on wheat, barley and oats is concentrated there. The present staff of the section, including two plant breeders working on maize at subsidiary stations, comprises eight graduate officers and additional supporting staff.

History records that the early settlers in Kenya started growing wheat at the beginning of the century; but that they suffered great loss due to rust attacks. Although a certain amount of desultory work was carried out from 1910 onwards, it was not until 1928 that wheat-breeding was put on an organized basis as a result of the visit of the late Sir Rowland Biffen, and the advice he gave to the Government to set up a wheat-breeding station. In that year the original station was built at Njoro and the late Capt. J. G. L. Burton, one of Biffen's pupils, was appointed to the first post of plant breeder. He was assisted by Mr. R. J. Lathbury, who later took charge when Burton retired. The Station has, until recently, remained virtually unchanged since those early days.

The present period of expansion dates from 1952–53 when development funds were first made available. The provision of improved facilities had become especially necessary due to the severe outbreaks of rust causing great damage to existing wheats and the urgent need to produce resistant varieties. The development has entailed recruitment of extra staff, purchase of additional land and specialized equipment, and now the construction of the new laboratories. It is especially satisfactory that farmers themselves, by agreeing to a cess on wheat, have made a substantial contribution to this development. Certain further projects, however, connected with rust pathology and maize breeding await the grant of special funds.

The plant breeding team is fortunate in being provided with such excellent new laboratories and modern facilities. Indeed, these are essential to the necessary intensification of the research programme to provide the rust-resistant wheats Kenya so urgently needs.

THE GALACTIC SYSTEM AS A SPIRAL NEBULA

THE view that the Galaxy might have a spiral structure has been expressed almost since the first discoveries of such structure in nebulæ. It was not until 1951, however, that part of the galactic spiral structure was actually found. Work in this field has recently been summarized in a report on the progress of astronomy by J. H. Oort, F. T. Kerr and G. Westerhout (*Mon. Not. Roy. Astro. Soc.*, 118, 379; 1958). The first definite discovery of spiral structure was accomplished by W. W. Morgan, S. Sharpless and D. E. Osterbrock, using the luminosity criteria for *O* and *B* stars developed by Morgan. They determined the distances of groups of these stars, and they showed that the regions of ionized hydrogen excited by the stars were arranged in long chains which formed parts of spiral arms. By a remarkable coincidence, radiation on 21-cm. wave-length from interstellar hydrogen was detected at about the same time as the visual work was done, and by 1954 a comprehensive picture of the spiral structure of the Galaxy could be assembled from radio observations. The importance of hydrogen-line radiation at 21 cm. arises partly because of the transparency of interstellar dust to radio waves and partly because the study of this radio spectrum line gives discrimination in distance. Actual distances can only be inferred from radial velocities, and this involves the assumptions of circular motion and of equality of motions of stars and gas in any particular region of the Galaxy.

In order to transform radial velocities into distances, we must know how the circular velocity in the Galaxy varies with the distance from the galactic centre, and we must know the distance of the Sun from the centre. If we know the distance and circular velocity of the Sun we can derive, from the radio observations themselves, the variation of circular velocity with distance from the centre for distances smaller than that of the Sun. The distance from the Sun to the centre has been obtained directly from the study of the distribution of cluster-type cepheid variables concentrated near the centre. The best estimate obtained in this way is 8·2 kiloparsecs, the accuracy being limited by the uncertainty in the interstellar absorption and in the absolute magnitude of the variables. The circular velocity, and an independent estimate of the solar distance, can be obtained by combining radio observations with the constants of differential galactic rotation obtained from the proper motions and radial velocities of distant stars. The best available estimate of the circular velocity of the Sun is 215 km./sec. For regions of the Galaxy farther from the centre than the Sun we cannot determine the rotational velocities from radio observations, and we must rely on values computed from models of the Galaxy based on stellar densities. The rotation curve derived by M. Schmidt from all available data shows a maximum of about 225 km./sec. at a distance of 7 kiloparsecs from the centre.

From profiles of the 21-cm. line one can now derive the density distribution of the neutral hydrogen in the Galaxy. Most of the hydrogen is confined to a flat disk, with a half-density whole-width of 220 parsecs. This hydrogen disk is remarkably flat; nowhere within 8 kiloparsecs from the centre do the points of maximum hydrogen density deviate by more than 75 parsecs from the galactic plane, although there are rather larger deviations in the outermost parts of the Galaxy. In contrast to this arrangement about the galactic plane the distribution in the plane shows great irregularities. The hydrogen outlines the spiral arms of the Galaxy. The Sun is situated near the inner edge of one arm; the latter probably contains the Orion association, and the whole arm is now called the Orion arm. Outside this, at a distance from the galactic centre of between 10 and 12 kiloparsecs, there is a conspicuous arm, called the Perseus arm, which contains the double cluster in Perseus. Inside the Orion arm, between 6 and 7 kiloparsecs from the centre, there is the Sagittarius arm. The hydrogen disk appears to terminate at about 15 kiloparsecs from the centre. The maximum density of hydrogen in the spiral arms is about 2 atoms/cm.^{3}; between the arms the density may fall to less than 0·05 atoms/cm.^{3}. These results are all compatible with the classification of the Galaxy as a spiral nebula of Hubble's type *Sb*. It is estimated that about 2 per cent of the total mass of the Galaxy exists in the form of interstellar gas. In the central region there is an arm at a distance from the centre of 3 kiloparsecs. The arm passes between the Sun and the centre, and in addition to participating in galactic rotation, this arm appears to be expanding with a velocity of 53 km./sec. away from the centre. This arm can be seen in absorption against the source Sagittarius *A* situated at the galactic centre. The existence of this expanding arm (and of other smaller features which are expanding) renders the rotation curve quite uncertain near the galactic centre.

The astounding flatness of the galactic interstellar medium is of importance in connexion with the internal motions in the medium. It provides a measure of the average random motion of the interstellar clouds, and it indicates that there must have been a considerable exchange of momentum from the inner to the outer parts of the disk. A fundamental question is whether spiral structure is a problem of gas dynamics (and magnetic fields) or of stellar dynamics. There seems no doubt that the spiral structure of galaxies is closely related to their content of interstellar gas, and the latter may be a prerequisite for spiral structures to develop. Supergiants and other young stars are situated in the spiral arms; there is as yet little evidence relating to the distribution of older stars and gas. The Galaxy rotates in a period of about 200 million years, and the effects of differential galactic rotation would severely distort any existing arms. The arms must either be smoothed out and replaced within this time or be maintained by some unknown mechanism independently of galactic rotation. There are reasons for believing that interstellar magnetic fields must be involved in such a mechanism. Interstellar polarization of the light of distant stars indicates the presence of magnetic fields, in many cases along the spiral arms. Part of the continuous radio emission from the Galaxy is closely concentrated in the galactic plane, and must be connected with spiral structure; the radiation appears to be of non-thermal origin, and may originate in synchrotron radiation from electrons moving in interstellar magnetic fields. The existence of radio coronae of the Galaxy and of the Andromeda nebula also supports the idea of the importance of magnetic fields. Nevertheless, we are forced to the conclusion that we have made little progress towards understanding the origin of spiral structure. We have, however, a much-improved knowledge of what has to be explained.

R. H. GARSTANG

IODINE AND COPPER UPTAKE BY SOIL ORGANIC MATTER

By J. M. NORTHMORE

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ALTHOUGH the soil organo-metallic complex concept of Bremner *et al.*[1] has been confirmed by the work of Beckwith[2], these workers do not specify the nature of the organic component of the complex. However, the relationship found between the replacement capacity of soil organic matter and its phenolic hydroxyl group content[3] points to material derived from lignin containing these groups being the organic component concerned. These considerations have led to an investigation of the relationships between the phenolic hydroxyl group content and the organo-metallic complex-forming capacity of the organic matter of a number of limed and unlimed soils from the Kenya Highlands. Wide ranges of *p*H values and organic matter contents were covered.

The phenolic hydroxyl group contents of the organic fractions of the soils were measured by the iodine uptakes according to the hypoiodite method of Norman and Peevy[4] as modified by Moodie[5]. The capacities of the same organic fractions to form organo-metallic complexes were measured by their copper uptakes by Lees's method[6] slightly modified.

Copper was taken as the complexing metal as it is known to have a greater ability to compete for sorption sites on organic matter than most of the other bivalent metals present in soil[2,7]. Preliminary investigations of the copper uptakes have indicated the possibility that added copper is preferentially absorbed by the organic fraction of a soil, and it is intended to offer evidence of this at a later date. Table 1 gives the copper and iodine uptake values obtained for the twelve soils studied.

The results show that increasing amounts of copper are taken up by the soil organic fractions with increasing *p*H values, the relationship between the two variables being curvilinear. No correlation

Table 1. IODINE AND COPPER UPTAKE BY SOIL ORGANIC MATTER

Soil	Total carbon (per cent)	Lime applied	*p*H	Copper uptake (m.equiv./gm. C)	Iodine uptake (m.equiv./gm. C)
*K*27	2·76	No lime	4·74	0·215	5·19
*K*20	2·86	4,400 lb./acre in 1953	5·16	0·268	4·55
*K*5	2·86	8,150 lb./acre in 1953	5·45	0·304	4·72
*K*48	2·53	17,740 lb./acre in 1953	6·12	0·735	4·35
*M*6	4·29	No lime	4·96	0·221	4·97
*M*8	4·22	15,000 lb./acre in 1954	6·01	0·628	4·76
MF	4·31	No lime	5·63	0·418	5·55
*MG*38	3·58	No lime	5·92	0·708	5·63
*MG*36	5·62	No lime	5·74	0·386	4·86
*ML*19	5·39	No lime	5·38	0·290	5·35
*ML*16	4·93	No lime	5·47	0·382	5·49
*E*127	2·44	No lime	5·45	0·409	5·62

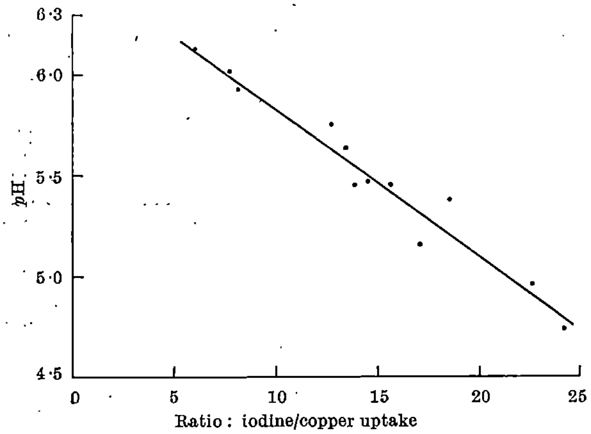

Fig. 1. Relation between pH and the ratio iodine/copper uptake by organic matter of some Kenya soils

is found between pH and iodine uptake. However, if the ratio iodine/copper uptake is plotted against pH then a rectilinear relationship results (Fig. 1), the regression equation of which is given by :

$$R = 90{\cdot}58 - 13{\cdot}85\, p\text{H} \quad (r = 0{\cdot}977)$$

A possible explanation of these results is suggested as follows.

It has long been thought probable that when the soil organic matter is treated with alkali, the compounds of high molecular weight undergo breakdown into smaller units, and it does not seem unreasonable to expect that at low concentrations of alkali the extent of this breakdown will depend upon the strength of alkali used.

If this effect can be extended to the action of lime in the field it might be expected that breakdown will occur with liming and the size of the organic structures existing in soil organic matter will be controlled by the pH of the soil. It has been shown that for the twelve Kenya soils studied, covering a fairly wide range of pH and total carbon values, a rectilinear relationship exists between pH and the ratio iodine/copper uptake. This relationship is taken as reflecting a close connexion between soil pH and the molecular complexity of its organic matter. The copper uptake, being determined at the pH of the soil, would be stoichiometrically proportional to the molecular compounds existing at that pH, and the iodine uptake, which is determined in the presence of 3 N sodium hydroxide solution, would be stoichiometrically proportional to the components of the compound. Therefore, the ratio of iodine/copper uptake would be a measure of the complexity of the molecular compound existing at that particular soil pH.

Evidence of the relationship between the copper- and the iodine-absorbing fractions of soil organic matter and the increase in copper absorption as compounds of high molecular weight are broken down into their constituent units when treated with alkali was obtained by treating four of the soils with concentrated ammonia. Excess ammonia was removed by drying followed by leaching with 0·5 M sodium sulphate solution. The copper uptake of the treated soil combined with the amount of copper required to precipitate the copper-precipitable constituents of the leachate was found to be much greater than the copper uptake of the untreated soil and to approximate to its iodine uptake (Table 2).

Table 2. Copper Uptake of Ammonia-treated Soil Organic Matter

Soil	Copper uptake untreated soil (m.equiv. Cu/gm. C)	Copper uptake of ammonia-treated soil (m.equiv. Cu/gm. C)	Iodine uptake (m.equiv. I/gm. C)
*K*5	0·304	4·72	4·72
*M*8	0·628	3·97	4·76
*ML*16	0·382	3·31	5·49
*K*48	0·735	5·06	4·35

The narrowing of the iodine/copper ratio with the increase of pH resulting from liming would appear to reflect a breaking down of soil organic complexes with parallel increase in mobility which may be of great importance in accounting for a number of the observed effects of liming.

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STRUCTURE OF ANHYDROUS SODIUM SOAPS AT HIGH TEMPERATURES

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THE present work is part of a systematic investigation of the liquid-crystalline structure of association colloids[1].

It is well known that anhydrous sodium soaps exhibit five liquid-crystalline allotropic phases at temperatures in the range 100–320° C. ; the transition points have been determined by different techniques[2], in particular, light transmission measurements, microscopic examinations under polarized light and dilatometric observations. The names of the phases and the transition temperatures are given in Table 1, taken from the paper by M. J. Vold, M. Macomber and R. D. Vold[3].

H. Nordsieck, F. B. Rosevear and R. H. Ferguson[4] have studied the different phases of sodium palmitate

Table 1

Name	Sodium laurate (C_{12})	Sodium myristate (C_{14})	Sodium palmitate (C_{16})	Sodium stearate (C_{18})
Subwaxy	100° C.	107° C.	117° C.	117° C.
Waxy	141	141	135	132
Superwaxy	182	176	172	167
Subneat	220	217	208	198
Neat	255	245	253	257
Isotropic melt	336	310	295	288

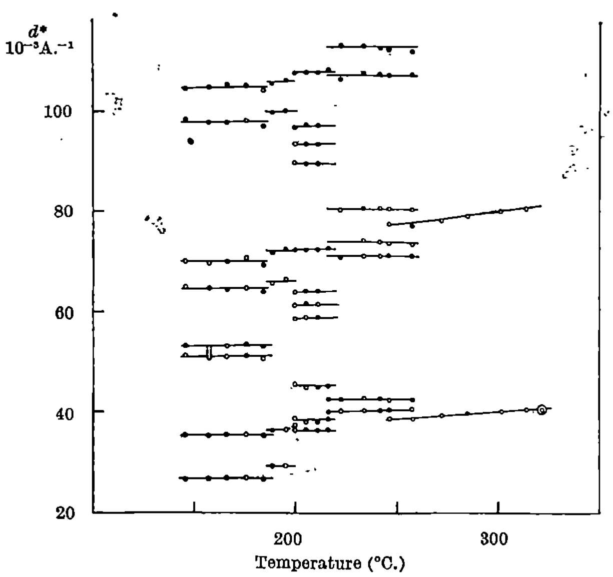

Fig. 1. Reciprocal spacings as a function of temperature for sodium laurate

by X-ray diffraction techniques. They recognized two main regions in the X-ray diagrams: the central part (0·01 A.$^{-1}$ $< s <$ 0·10 A.$^{-1}$; where $s = 2\sin\theta/\lambda$), where they observed several sharp lines, and a region in which s is of the order of 0·25 A.$^{-1}$, where they found one or two diffuse bands. They considered the position and the profile of the bands as evidence that the soap molecules are packed in a hexagonal array and rotate freely around their axes. These authors did not try to determine the crystal lattices responsible for the sharp lines.

An infra-red absorption study[6] has shown that in all the high-temperature phases, from the subwaxy to the isotropic melt, the paraffin chains are disordered and that their configuration is similar to that of a paraffin liquid.

The purpose of our investigation was to determine the liquid-crystalline structure of the different phases of sodium laurate, myristate, palmitate and stearate, by the interpretation of the sharp lines occurring in the central region of the X-ray diagrams.

We have used a Guinier-type focusing camera, which was evacuated and provided with a bent quartz monochromator. The samples were held in an electric furnace and the temperature was maintained with an accuracy of 0·5 deg. C. The soaps were produced by neutralizing alcoholic solutions of the fatty acids (supplied by the Eastman Kodak Co.). Water and alcohol were eliminated by heating the sample for 1–2 hr. *in vacuo* at 120° C. in the cell in which it was enclosed for the X-ray investigations. These precautions for avoiding water and alcohol seem to be sufficient, since X-ray diagrams show no appreciable dependence upon moisture.

We have taken at least one hundred X-ray diagrams of each soap in the temperature-range 100–350° C. In the central part of the diagrams we have observed a large number of sharp diffraction lines (sometimes more than twenty). These sharp lines form a typical pattern for every phase; the transition temperatures are in good agreement with those previously determined (see Table 1). We have plotted in Fig. 1 some of the experimental results for sodium laurate.

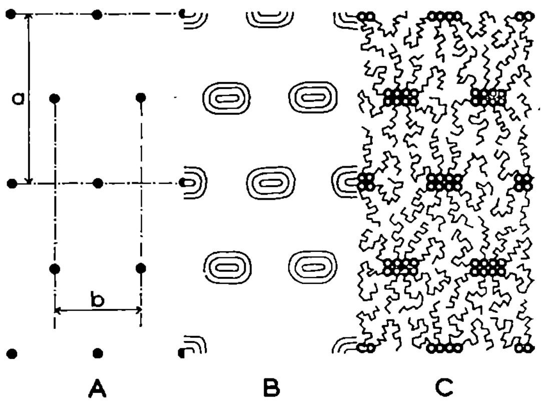

Fig. 2. (*A*) Two-dimensional centred rectangular lattice. (*B*) Electron-density projection along [001]. Contours are at equal arbitrary intervals, with the zero contour omitted. (*C*) Schematic structure of the rectangular phases

At s of the order of 0·2–0·3 A.$^{-1}$, the diagrams show the diffuse bands described by Ferguson and co-workers[4]; but we have observed that at low temperatures (more particularly in the subwaxy and the waxy phases) the bands have a fine structure, which is the more detailed the lower the temperature.

Since the experimental results are essentially the same for the four soaps investigated, we propose to describe separately the structure of every phase.

Subwaxy, waxy, superwaxy, subneat. The observed spacings are consistent with a two-dimensional centred rectangular lattice (space group $c2mm$; ref. 5) (see Fig. 2*A*). By way of example, we compare in Table 2 the observed spacings (sodium laurate at 166° C.) and the calculated spacings for a rectangular cell with sides a = 75·2 A., b = 30·9 A.

Table 2

Indices $hk0$		200	110	310	400	020	220	130	330
s (in 10^{-3} A.$^{-1}$)	exp.	26·2	35·2	51·0	53·1	64·3	70·0	97·7	105·2
	calc.	26·6	35·0	51·4	53·2	64·7	69·9	97·9	105·0

The structure (see Fig. 2 *C*) consists of a set of parallel ribbons, indefinite in length, packed in the rectangular array. The polar groups of the molecules fit into the ribbons. The paraffin chains, in a liquid-like state,

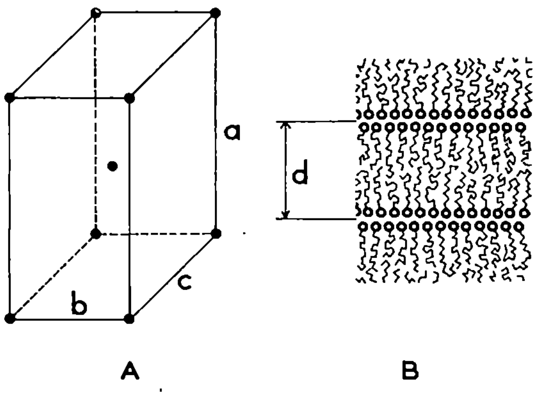

Fig. 3. (*A*) Bravais unit cell for the three-dimensional body-centred orthorhombic structure. (*B*) Schematic structure of neat soap

Table 3

Phase	Structure	Sodium laurate		Sodium myristate		Sodium palmitate		Sodium stearate	
Waxy	two-dimensional rectangular	166° C.	a = 75·2 A. b = 30·9 A.	155° C.	a = 80·0 A. b = 34·5 A.	152° C.	a = 86·6 A. b = 38·3 A.	140° C.	a = 80·0 A. b = 40·3 A.
Superwaxy	two-dimensional rectangular	195° C.	a = 68·5 A. b = 30·3 A.	193° C.	a = 69·0 A. b = 33·6 A.	195° C.	a = 74·2 A. b = 36·0 A.	198° C.	a = 72·5 A. b = 37·9 A.
New phase	three-dimensional orthorhombic	205° C.	a = 55·5 A. b = 28·3 A. c = 32·7 A.						
Subneat	two-dimensional rectangular	234° C.	a = 49·8 A. b = 27·0 A.	233° C.	a = 53·8 A. b = 29·1 A.	236° C.	a = 56·2 A. b = 30·6 A.	238° C.	a = 62·4 A. b = 34·4 A.
Neat	lamellar	290° C.	d = 25·3 A.	271° C.	d = 27·5 A.	278° C.	d = 29·1 A.	285° C.	d = 80·6 A.

fill up the rest of the cell. The intensities of the lines are in good agreement with this model; this is confirmed by the electron-density distribution calculated with the observed amplitudes and the signs corresponding to the model (Fig. 2 *B*).

The dimensions of the unit cell depend on the soap and on the phase; they are given in Table 3. For every soap, the higher the temperature the more symmetrical (closer to a hexagonal cell) is the shape of the unit cell.

Neat. In this phase the X-ray diagrams contain three or four lines giving Bragg spacings in the ratio 1 : 1/2 : 1/3 : 1/4, characteristic of a lamellar structure (one-dimensional lattice). The structure of the neat phase is sketched in Fig. 3 *B*.

The neat is the only phase in which the spacings are strongly dependent on temperature. The coefficient of linear thermal expansion is negative and its value approximately -5×10^{-4}/deg. C. (note that, at room temperature, the thermal expansion coefficient of the large parameter of crystalline soap is $+5 \times 10^{-5}$/deg. C.). We have observed the same thermal effect in the liquid-crystalline structures of soap–water systems[7] and we have interpreted it to mean that hydrocarbon chains are liquid-like in character.

Isotropic melt. X-ray photographs taken at a temperature a few degrees above the melting-point contain two or three fairly sharp bands corresponding to the Bragg spacings of neat soap. This observation suggests that the structure of the melt is quite similar to that of the neat phase.

A new phase. In sodium laurate, we have observed a new phase occurring between the superwaxy and subneat phases. This new phase does not seem to have been noticed by previous workers.

The lattice is three-dimensional body-centred orthorhombic, space group *Immm* (see Fig. 3 *A*); the dimensions are: $a = 55·5$ A., $b = 28·3$ A., $c = 32·7$ A. The spacings and intensities of the diffraction lines are in good agreement with a model in which the polar groups of the soap molecules pack into slightly asymmetrical disks, which pile up in the crystal, and the paraffin chains fill up the rest of the cell. This phase is not found in the other soaps.

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GENETIC CONTROL OF HUMAN HAPTOGLOBIN SYNTHESIS

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THE haptoglobins, a group of serum proteins that combine with hæmoglobin, were first studied by Jayle and his colleagues in Paris[1]. They showed that the complex of hæmoglobin and haptoglobin has peroxidative activity, and that this reaction can be used to assay haptoglobin in serum. Connell and Smithies[2] have developed a sensitive technique for analysing this peroxidase activity, using hydrogen peroxide as the oxidizing substrate and guaiacol as hydrogen donor.

The observations of the French workers suggested that at least two haptoglobin types exist. One (type II) was purified by fractional precipitation of the urine of a nephrotic child and shown[3] to be a glycoprotein of molecular weight about 85,000. The other haptoglobin (type I), purified from human serum, was reported[4] to have a similar composition and a molecular weight of about 160,000. It was concluded that type I might be a dimer of type II.

With the introduction of the starch gel technique of zone electrophoresis, Smithies[5] recognized three types of human sera, which were later[6] termed types 1–1, 2–1 and 2–2. It became clear that the proteins differing in the several serum types were haptoglobins[6], Jayle's type II haptoglobin corresponding to Smithies's 1–1, and Jayle's type I to Smithies's 2–2, respectively[7].

Smithies and Walker[6] offered a simple hypothesis for the inheritance of the haptoglobin types. They suggested that a single pair of allelic genes, Hp^1 and Hp^2, segregate in human populations, the three genotypes Hp^1/Hp^1, Hp^2/Hp^1 and Hp^2/Hp^2 corresponding to the phenotypes 1–1, 2–1 and 2–2, respectively. Other family studies[8] have confirmed that this is the usual mode of inheritance of haptoglobins. However, atypical segregation has been observed[9] and modified phenotypes reported[2,10]. Moreover, in some populations relatively high fre-

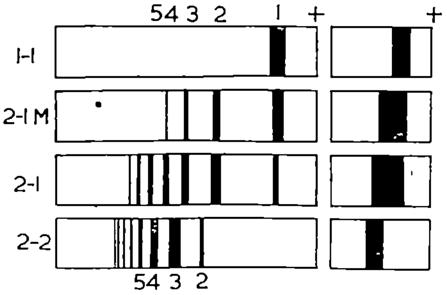

Fig. 1. Relative mobilities of haptoglobins and their complexes with hæmoglobin from the several phenotypes at *p*H 8·4, left, in starch gels, right, in starch blocks. The numbers show the supposed degree of polymerization of components and + marks the anodal side

quencies of individuals without demonstrable haptoglobins have been found[10,11]. These variations will be discussed below.

Bearn and Franklin[12] have recently studied haptoglobins and their complexes in the ultracentrifuge. In sera of type 1–1, haptoglobin was reported to have a sedimentation coefficient of 3–4 *S.*, increasing to 6 *S.* on addition of hæmoglobin, in agreement with the observations of Guinand *et al.*[3]. In the other serum types, haptoglobins and their complexes with hæmoglobin showed several peaks in the ultracentrifuge, most of those from type 2–2 sera having higher sedimentation coefficients than those from type 2–1 sera. In view of this complexity, and the numerous haptoglobin components demonstrated by starch gel electrophoresis of 2–1 and 2–2 sera[2,9,13], it was concluded that the genetical control of haptoglobin synthesis is "probably exceedingly complex". Moreover, since one of the components in the ultracentrifuge was present only in 2–1 sera, Bearn and Franklin suggested that the haptoglobin genes might interact in the heterozygote to produce a hybrid product like those described in doves[14] and rabbit[15] and human[16] blood groups.

This system is of unusual interest, then, in relation to the genetic control of protein synthesis, for not only does the heterozygous individual produce proteins different from those in either homozygous type, but also in two of the types the haptoglobins consist of several fractions. No other genetic system is known in which a single locus controls the specificity of more than one protein[17]. It therefore seems worth while to present a hypothesis for the genetic control of haptoglobin formation which brings this group of proteins into line with others and appears to provide an adequate explanation for all the findings so far reported.

The differences between haptoglobins in the three types will first be briefly recapitulated (Fig. 1). In type 1–1 sera only a single haptoglobin is present, having a relatively high mobility on filter paper and starch block electrophoresis and also in starch gels at *p*H 8·4–8·6[2,5,12,13]. Ultracentrifugal studies show only a single component of relatively low molecular weight[3,12]. Type 2–2 haptoglobins appear as a single component when submitted to electrophoresis on filter paper and in starch blocks, having a lower anodal mobility than type 1–1 haptoglobin. However, when 2–2 haptoglobins are submitted to electrophoresis in starch gels, numerous components, becoming fainter towards the origin, are resolved. Since these components do not differ in charge (as shown by the uniform mobility on filter paper and in starch gels), it is a reasonable inference that they differ in size, which is known to affect mobility in starch gels[18]. This inference is strengthened by their heterogeneity in the ultracentrifuge. Indeed, if the frictional coefficients of 1·4–1·6 calculated for purified haptoglobins[3,4] are taken together with sedimentation coefficients of 2–1 and 2–2 haptoglobins extrapolated to zero protein concentration[12], it seems likely that a polymer series is present. The lowest (4 *S.*) component, present only in 1–1 and 2–1 sera, would represent a monomer (molecular weight about 80,000), the second (6–7 *S.*) a dimer (molecular weight about 160,000), the third a trimer, and so forth, dimers and higher orders being present only in 2–1 and 2–2 sera. In 2–1 sera one haptoglobin component is identical in mobility in starch gel electrophoresis with the haptoglobin of type 1–1. Other haptoglobin bands consistently show a higher electrophoretic mobility in starch gels than the haptoglobins in type 2–2 sera. In modified type 2–1 sera (2–1 *M*), the first component is greater and the second component is smaller than usual, and very little of the other components is present; this type is especially common in Africans[10].

An attempt will now be made to provide an explanation for these seemingly confusing observations. It is suggested that recently synthesized haptoglobin molecules (of molecular weight about 80,000) have complementary combining sites (1 and 2) through which aggregation can take place under favourable conditions. The protein product of the Hp^1 gene is Hp1, which has only a single combining site (Fig. 2). Since the complementary combining site is lacking, only monomers are present in Hp^1/Hp^1 homozygotes. The product of the Hp^2 gene, which can be termed Hp2, has both complementary combining sites 1 and 2, and also a lower negative charge at *p*H 8·4 than Hp1. Hence in Hp^2/Hp^2 homozygotes the haptoglobin molecules can combine with one another, so that polymers are formed. It would appear that a small proportion of dimers, a high proportion of trimers and progressively lower proportions of tetramers and higher polymers result. The different polymers are separated by starch gel electrophoresis, so that numerous bands are seen, becoming progressively fainter towards the origin.

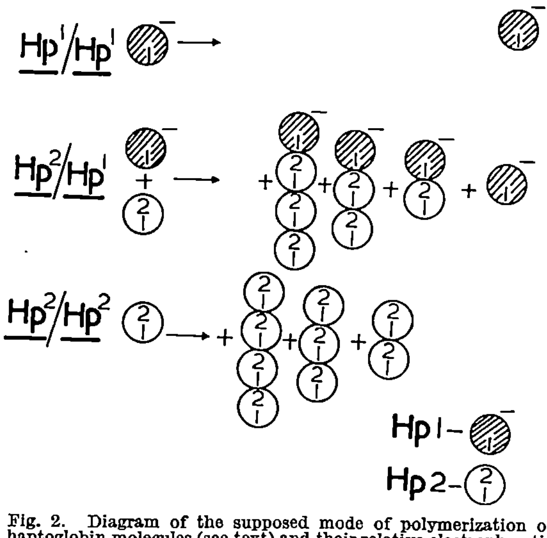

Fig. 2. Diagram of the supposed mode of polymerization of haptoglobin molecules (see text) and their relative electrophoretic mobilities in starch gels. Only the first three polymers are shown. Origin to the left and anode to the right. For convenience the polymers are shown as linear; in practice they are more likely to be globular

In heterozygotes, Hp1 and Hp2 molecules are formed side by side (like A and S hæmoglobins in sickle-cell heterozygotes). These form mixed polymers, each containing only one Hp1 molecule, which has a single combining site. The commonest polymer is the dimer, with progressively fewer trimers, tetramers and higher orders. Since Hp1 has a greater negative charge than Hp2 at pH 8·4, the mixed Hp1, Hp2 polymers would have a higher electrophoretic mobility than the polymers Hp2, Hp2 on both starch block and starch gel electrophoresis. However, in the absence of masking of charged groups, all Hp1, Hp2 polymers would have the same charge and therefore a similar electrophoretic mobility in starch blocks or on filter paper; and the same would be true of Hp2, Hp2 polymers. Nevertheless, if approximately equal proportions of Hp1 and Hp2 are formed in heterozygotes, all the Hp2 but only a fraction of Hp1 molecules will polymerize; hence the residual Hp1 molecules will form a component identical with Hp1 in Hp^1/Hp^1 homozygotes.

The genetic variant 2–1 M is readily explained by supposing that a higher proportion of Hp1 than usual is synthesized. There will therefore be more residual Hp1 monomer and less Hp1, Hp2 dimer than in type 2–1, with only very small proportions of higher polymers.

The genetic control of haptoglobin synthesis is analogous in some respects to that of the human hæmoglobin types. Hæmoglobins S and C differ from normal adult hæmoglobin (A) in charge: this appears to be due to the substitution of a valine or lysine residue for glutamic acid, respectively, in each half-molecule[19]. Although the differences between them are so small, S is the only hæmoglobin which polymerizes in the absence of oxygen into highly asymmetrical units, this process being responsible for sickling and birefringence of erythrocytes in susceptible subjects[20]. Moreover, hæmoglobin S can form mixed polymers with hæmoglobins C or A [20], in somewhat the same way that it is suggested that Hp2 molecules can form mixed polymers with Hp1. Here the analogy ends, for hæmoglobin polymers seem to be due to the formation of secondary intermolecular bonds which are easily disrupted, for example, by oxygen or urea[20]. The starch gel electrophoretic patterns of haptoglobins, on the other hand, suggest that the polymerization is relatively stable, being unaffected by the presence of 8 M urea and relatively wide changes of pH (1·7 to 9·0)[2,13]. Moreover, when the protein in one band is eluted from starch gels and again submitted to starch gel electrophoresis, it runs as a single component with its original mobility[2,13]. These results exclude metastable polymerization[21] and suggest that the haptoglobin polymers may be held together by primary bonds. The nature of the bonding is at present under investigation. If it proves possible to break down Hp2 polymers, the resulting monomers should, when mixed with Hp1 molecules in various proportions, yield 2–1 and 2–1 M patterns, thereby providing experimental confirmation of the hypothesis here advanced. It may also explain two further problems: why polymerization is limited in Hp^2/Hp^2 subjects, so that low-order rather than higher-order polymers occur, and why Hp1 does not interact (at any rate, rapidly) with Hp2, Hp2 polymers when they are mixed[12,13].

The other genetical problem posed by the haptoglobins is the presence in several populations of persons without demonstrable haptoglobins, to which attention was directed by Allison *et al.*[11]. A number of sera have now been re-tested by the sensitive peroxidase technique of Connell and Smithies[2]. Only two British sera out of a total of 632 examined over a period of four years have failed to show haptoglobins by electrophoretic or peroxidative analysis. On the other hand, no haptoglobins could be demonstrated by the peroxidase reaction in 14 out of 20 sera from West Africans previously thought to be ahaptoglobinæmic.

The question then arises whether lack of haptoglobins in these subjects could be secondary to hæmolytic anæmia or liver disease[22,23]. This seems unlikely. The British subjects without haptoglobins on repeated tests were apparently healthy adults, with normal blood counts; and similar observations on British subjects have been presented by Harris *et al.*[8]. The Africans studied were also apparently healthy adults, who should have had considerable resistance to malaria. Ahaptoglobinæmia in Africans was not correlated with the presence of abnormal hæmoglobins S or C, which in the heterozygous condition are not associated with low haptoglobin levels, although absence of haptoglobins has been reported in patients homozygous for abnormal hæmoglobin genes[22]. Furthermore, the recent demonstration by Giblett[10] that some American Negroes lack haptoglobins rules out the possibility that ahaptoglobinæmia is always secondary to malaria, malnutrition, liver disease or other factors in the African environment.

It seems likely, then, that a small proportion of Caucasians and a higher proportion of Africans congenitally lack haptoglobins. In some cases, at least, this does not seem to be due to homozygosity for a third, 'silent' allele at the Hp locus. Mothers of ahaptoglobinæmic subjects who have been of phenotype 2–1 could not have been carriers of the silent alleles[8,9,13], on the hypothesis here advanced or any other plausible hypothesis. The most likely genetic explanation for ahaptoglobinæmia seems to be homozygosity for a recessive suppressor gene at another locus[8,9,22], but further family studies would be desirable.

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

Calculation of Erosion in Space from the Cosmic-Ray Exposure Ages of Meteorites

VERY little is known about erosion in space—the action of dust, gas, ions and electrons in wearing away material from exposed surfaces in interplanetary space. A cosmic-ray exposure age is obtained from the measurement of one radioactive and one stable spallation isotope produced in a meteorite by cosmic rays. A new interpretation of this age indicates that it sets an upper limit to the erosion-rate of a meteorite in space. The more obvious interpretations in terms of meteoritic break-up and planetary perturbational effects may remain valid.

The cosmic-ray exposure age is determined from the spallation isotope content of a meteorite, with the assumption that the spallation-rate does not vary with time. If erosion occurs in space, however, the spallation-rate in the distant past would have been smaller than in recent times because of the greater amount of shielding material. Hence, due to erosion in space, the measured cosmic-ray exposure age is less than the interval since the meteorite was exposed to cosmic rays. Consequently, the cosmic-ray exposure age gives an upper limit to the rate of erosion in space.

We shall base our discussion on the argon exposure age[1] of the Sikhote–Alin meteorite. The value of 5×10^8 years was obtained[1] from the number of argon-38 atoms (stable isotope) and the decay-rate of argon-39, a radioactive isotope with a half-life of 260 yr. The tritium (helium-3) ages of two iron[2] and one stone[3] meteorite have also been measured; however, the argon exposure age is subject to fewer uncertainties than the tritium (helium-3) age.

We shall assume that the rate of production of argon-38 near the centre of a large iron sphere of radius R obeys the attenuation rule:

$$\mathrm{d}^{38}\mathrm{A}/\mathrm{d}t = C \exp(-R/72) \text{ for } R \geqslant 100 \text{ cm.}$$

where C is a constant determined by the spallation properties of the iron nucleus and the cosmic ray flux.

The Sikhote–Alin meteorite was quite large: the argon-39 radioactivity in the measured sample was about one-ninth the activity expected in a small unshielded body. If the rate of erosion in space is designated by E and if r is the radius of the meteorite just before it struck the atmosphere, then the rate of production of argon-38 at t years ago was $C \exp\{-(r + Et)/72\}$. The present rate of production is $C \exp(-r/72)$. The measured cosmic-ray exposure age, 5×10^8 yr., is given by the expression $\int_0^T (\mathrm{d}^{38}\mathrm{A}/\mathrm{d}t)\mathrm{d}t/C \exp(-r/72)$, where T is the time that the meteorite existed as a body exposed to cosmic rays. If the attenuation rule is substituted into this expression, then the following relation is obtained:

$$5 \times 10^8 \text{ years} = (1 - \exp(-Et/72)/(E/72)$$

where E is the rate of erosion.

Since the time T is greater than the measured exposure age, 5×10^8 years, the upper limit to the rate of erosion E is $1{\cdot}5 \times 10^{-7}$ cm./yr. for an iron meteorite. This rate is somewhat smaller than an estimate made by one of us (F. L. W.)[4].

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Observations of the Lithium Lines in the Twilight Airglow in the Northern Hemisphere

THE recently published discovery of the lithium resonance line in the twilight airglow by Delannoy and Weill[1] and further observations of the emission by Gadsden and Salmon[2] have led to a discussion as to the origin of the lithium atoms in the upper atmosphere. Barbier, Delannoy and Weill[3] have considered the possibility of marine and meteoric origins for the lithium and have favoured the latter hypothesis because the derived abundance ratio lithium/sodium agreed better with the ratio for the meteoric material. Donahue[4] has suggested that the lack of linearity in the relation between sodium brightness and abundance could make ambiguous any conclusions based on the lithium/sodium brightness ratio alone. A third possibility suggested by the U.S.A. International Geophysical Year Committee[5], and supported further by Barber[6], is that the lithium originates from 'hydrogen' bomb tests at high altitude; it is suggested, in particular, that the high-altitude Johnston Island test of August 1, 1958, was responsible for the lithium emissions reported by Gadsden and Salmon from Antarctica and New Zealand. In view of the uncertainty of present knowledge of the behaviour of the lithium emission, an observation from a station in the northern hemisphere should be of interest.

Twilight spectra covering the region 6000–7000 A. have been obtained at Saskatoon regularly since January 1959. An $f/0{\cdot}8$ auroral grating spectrograph[7] was used to photograph the spectrum on Kodak 103 *a–F* plates. During the exposures the spectrograph was guided according to an exposure programme which kept it pointing at the point in the Sun–zenith plane where the geometrical shadow height was 80 km. Following such a programme, a 30-min. exposure may be obtained during a single twilight with a zenith angle range of 0–83°.

A very weak lithium line was obtained in this way on a plate exposed on four occasions during clear twilight during the period January 10–21, 1959. The total exposure time was 115 min. Comparison of this spectrum with the spectrum of a calibrated source of low brightness led to a value of 30 rayleighs for the zenith brightness of the lithium emission for a height of 80 km. of the geometrical shadow.

An estimate of the abundance of lithium in the upper atmosphere can be made from the observed brightness. First the brightness when the lithium layer is fully illuminated must be estimated. The correction factor required depends on the distribution of the lithium with height. A value of about 5 for this correction factor was obtained by assuming the lithium distribution to be the same as that for sodium and then applying the theory developed by Hunten[8] to calculate a theoretical relation between brightness and geometrical height of shadow. A value of 150 rayleighs is thus estimated for the maximum zenith brightness when the lithium layer is fully illuminated by the Sun. The rate coefficient for the resonance fluorescence process for lithium obtained from the standard equation[9] is 17 photons/sec. per illuminated atom. This leads to the conclusion that the lithium abundance over Saskatoon in January was about 9×10^6 atoms/cm.^{2}. The sodium abundances estimated for the same period of observation from data kindly provided by Dr. D. M. Hunten may have been as high as 20×10^9 atoms/cm.^{2}. Consequently, the lithium – sodium abundance ratio was about 45×10^{-5} compared with 200×10^{-5} for meteors and $2 \cdot 3 \times 10^{-5}$ for sea water. If ionization is taken into account[3], it is possible that the abundance ratio derived from our measurements should be somewhat higher.

This result for the lithium – sodium abundance ratio, neglecting ionization, falls between the values for sea water and meteors, and cannot be considered as decisive evidence against either hypothesis in view of the uncertainties of the measurement. Moreover, since the chemical and physical properties of lithium and sodium (and their compounds) are considerably different, it is by no means certain that the abundance ratio in the upper atmosphere should be close to that of the source. As to the possibility of the lithium arising from bomb tests, it is possible that the lithium detected above Saskatoon in January is a remnant of that introduced into the atmosphere last August. However, it is also possible that the brightness of the emission in the southern hemisphere in August and September is associated with a seasonal variation of the lithium abundance; this abundance might well show a maximum about 2½–3 months after midwinter, as is the case for sodium in the northern hemisphere[10]. This question can be determined only by further systematic measurements.

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Sub-surface Temperatures on the Moon

RECENTLY, Fremlin[1] has suggested that craters on the Moon may be filled with dust to considerable depths and that extremely high temperatures may be attained in them. While the effects described by him must exist, it should be pointed out that the extreme values he predicts are obtained by using a value for the thermal conductivity of the dust which is probably much too low and combining with this a value of the heat flux which is probably much too high. These points will be discussed in order.

Information about the thermal conductivity near the surface is obtained from optical and radio micro-wave observations of the variation of the surface temperature during an eclipse or throughout a lunation. These yield a value of $(K\rho c)^{-1/2}$, where K, ρ and c are the thermal conductivity, density and specific heat of the material near the surface (assumed to be independent both of temperature and depth). The optical eclipse observations of Pettit and Nicholson[2] were first reduced by Epstein[3], who deduced a value of 120 for $(K\rho c)^{-1/2}$, the units being C.G.S., calorie and degrees centigrade; since this is much higher than that for solid rock (about 20) he attributed it to a covering of 'pumice' or volcanic ash. Later, using more refined analysis and discussing both the variation of surface temperature during an eclipse and throughout a lunation, Wesselink[4], Jaeger and Harper[5], Lettau[6] and Jaeger[7] showed that Epstein's value was too low and independently obtained values of $(K\rho c)^{-1/2}$ of the order of 1,000. Similar values were obtained by Piddington and Minnett[8] and Jaeger[9] from the radio micro-wave observations. Taking $\rho = 2$, $c = 0 \cdot 2$, this corresponds to $K = 2 \cdot 5 \times 10^{-6}$: this low value was attributed to dust from meteoritic or other sources.

The agreement with experiment of calculations based on the above assumptions is good but by no means perfect, and all writers have recognized that it could be improved if the conductivity increased with either depth or temperature. In the absence of knowledge of a likely law of the variation of conductivity with temperature, discussion has been concentrated on the variation with depth, and it has been shown[5,8,9] that a rather better fit is obtained with a model consisting of a few millimetres of dust with $(K\rho c)^{-1/2} = 1{,}000$ resting on a substratum with $(K\rho c)^{-1/2} = 120$. This substratum might be composed either of tuffaceous material of volcanic origin or of material composed of rock fragments of all sizes produced by erosion due to thermal stresses. Recently, Muncey[10] has obtained a better fit with the radio micro-wave observations with a model in which both K and c are proportional to the absolute temperature with a value of $(K\rho c)^{-1/2}$ of 200–300 at 300° K. This low value, however, is inconsistent with with the optical eclipse observations, since it gives temperatures in the umbral phase which are about 60 deg. too high.

Taking $\rho = 2$, $c = 0 \cdot 2$, the discussion above leads to a conductivity of the order of $2 \cdot 5 \times 10^{-6}$ at the surface, increasing in a few millimetres to 2×10^{-4}. These figures may be compared with the value of $7 \times 10^{-7} h^{1/2}$, where h is the depth below the surface, used by Fremlin. If this value 7×10^{-7} at a depth of 1 cm. were used for the surface conductivity, it would give calculated values of temperatures in the umbral phase of a lunar eclipse which are 25 deg. K. too low.

Turning to the values for the lunar heat flux used by Fremlin, he assumes that the average rate of heat production over the volume of the Moon due to radioactivity is that of 2 p.p.m. of uranium, corresponding to a total heat production of about 10^{20} cal./year. If the whole of this heat is lost by radiation from the surface, the surface heat flux would be $8 \cdot 4 \times 10^{-6}$ cal./cm.^{2} sec., which is seven times the terrestrial value. There is good evidence (Birch[11]) that the average rate of production of heat in the Earth is nearly the same as that of the chondritic meteorites, the total rate of production of heat in the Earth being of the order of $2 \cdot 3 \times 10^{20}$ cal./year, or not much more than twice that assumed by Fremlin for the Moon ; if the whole of this heat were radiated from the surface, the surface heat flux would be $1 \cdot 4 \times 10^{-6}$ cal./cm.^{2} sec., which is in good agreement with the observed value of $1 \cdot 2 \times 10^{-6}$. An average heat production in the Moon at the chondritic rate would give a lunar surface heat flux of the order of $2 \cdot 3 \times 10^{-7}$ cal./cm.^{2} sec., and this is the value which probably should be assumed in the absence of evidence to the contrary. If the production of heat at the rate assumed by Fremlin were distributed over the volume of the Moon, melting would occur in a relatively short time : if, by a process of differentiation, it were concentrated into a crustal layer, not only would the concentration of radioactive elements near the surface be higher than in any terrestrial rocks, but, again, melting temperatures would be reached at shallow depths even in the absence of any blanketing dust. The triaxial figure of the Moon requires that there should have been substantial strength in the interior for a considerable time in the past.

Whether the blanketing effect described by Fremlin, which undoubtedly must exist, is of importance or not depends entirely on the values assumed for the conductivity and the lunar surface heat flux. Neglecting time effects in blanketing, lateral flow to better conducting regions, and the fact that the Moon is not in thermal equilibrium, all of which tend to reduce the magnitude of the effect, Fremlin deduces an excess temperature of 1,200° C. at a depth of 25 m. ; with the same high heat flux and the conductivity of 2×10^{-4} deduced for the substratum from the eclipse observations, this figure would be reduced to 105° C. For a heat flux of the terrestrial value, $1 \cdot 2 \times 10^{-6}$ cal./cm.^{2} sec., the corresponding results would be 170° C. and 15° C. ; while with the flux of $2 \cdot 3 \times 10^{-7}$ cal./cm.^{2} sec. corresponding to the chondrite model they would be 33° C. and 3° C., respectively.

Finally, it should be said that this matter is just within the range of experiment. Since the optical effects arise from a thin layer near the surface while the radio waves originate from a region some metres in thickness, the mean temperature as shown by micro-waves should be greater than that derived from optical observations if there is any general increase of temperature with depth due to the lunar heat flux. Using Fremlin's value $24\sqrt{h}$ for the temperature at depth h and a value $\alpha = 0 \cdot 025$ given by Piddington and Minnett[8] for the micro-wave attenuation coefficient α, the difference between the mean temperatures deduced from micro-wave and optical observations should be 135 deg. C. This figure is probably far too low, since the value of α used is of the order of that for dry soil and the attenuation for lunar surface material should be much lower. This calculation provides an independent indication that the temperatures deduced by Fremlin are much too high. But there is some evidence that the mean micro-wave temperature is a few degrees higher than the mean optical temperatures and a careful analysis might lead to information about the lunar heat flux.

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Prof. Jaeger is quite right in pointing out that I have used a high figure for the radioactivity of the Moon, and also that my value for conductivity near the surface is lower than the mean value calculated from observations. This does not necessarily prove that my values are wrong. I assume Kozyrev's observations of hot gases to be reliable. They would not have been expected on the basis of conventional views of lunar characteristics and presumably, therefore, conventional views must be modified. I have suggested some modifications, which may easily be wrong. The more conservative of Prof. Jaeger's figures, however, must almost necessarily be wrong. They show that phenomena observed by Kozyrev could not have occurred.

I do not think that there is a contradiction between my figures for conductivity and experiments done so far. My whole argument is based on the idea of large thicknesses of dust in specific limited areas. Measured radiation from the lunar surface has been averaged from considerable areas (in the micro-wave work, nearly the whole of the Moon's disk) within which any bare rock would be expected to have a thermal conductivity very much higher than the mean value observed. Small areas of high conductivity could have a large effect on the calculated average temperatures on the dark side of the Moon. Their increasing share of the total radiation at the lower average temperatures might quite possibly explain the small divergence shown between Pettit's infra-red observations during a lunar eclipse and Prof. Jaeger's calculations (his reference 9, Fig. 1). These calculations show the apparent variations of temperature with time to be expected for a uniform lunar surface with values of $(K\rho c)^{-1/2}$ from 20 (bare rock) to 1,370. The calculated temperatures fall too fast in the umbral phase. Instead of assuming inhomogeneity with depth, let us assume the existence of two types of surface, one bare rock ($K\rho c^{-1/2} = 20$) and one a dust ($K\rho c^{-1/2} = 2,700$) of about five times lower conductivity than the mean value giving best agreement. Then we can get an almost exact fit with Pettit's observations if the bare rock covers 4·8 per cent of the total area—a not unreasonable result. (The two volumes of conductivity are quite arbitrary, having been chosen simply to make computation from Prof. Jaeger's calculations as easy as possible.) If we do not limit ourselves to two kinds of surface only, or if we allow for a difference of albedo, there would be no difficulty in accommodating adequate areas of conductivity well below even those assumed in my original communication.

It is in any event difficult to believe that the alternative picture suggested by Piddington and Minnett, of a uniform 1-mm. layer of dust, over mountain-side and plain alike, can be more than a convenient analytical model.

With regard to the supposed radioactivity, I am on weaker ground. I had failed to consider the need for high mechanical strength to maintain the observed shape of the Moon, and I am grateful to Prof. Jaeger for pointing this out. It is clear that the average lunar radioactivity must be well below that given for the Earth's crust, unless the thermal conductivity of the solid lunar rock is a good deal higher than hitherto supposed. The obvious way out is to suggest a non-uniform distribution of radioactive material. The likelihood of this depends on what we assume about lunar history, which seems too large a subject to discuss here.

My main contention remains: that I am willing to feel doubt about any of my assumptions, but am unwilling to give up the entire picture until an alternative explanation of Kozyrev's observation is given.

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Magnetostriction and Palæomagnetism of Igneous Rocks

In a recent communication, Stott and Stacey[1] report on a "crucial experiment" from which they conclude: "This excellent agreement between the dip and the directions of artificial thermoremanent magnetization of the stressed and unstressed rocks indicates that large systematic errors due to magnetostriction are most improbable in igneous rocks of types normally used for palæomagnetic work". This experiment was intended to test the proposals[2] and measurements[3] bearing on the role of magnetostriction in rock magnetism. We present here our reasons for believing that the experiment was not crucial and that the conclusion is not justified.

The magnetic fraction of natural igneous rocks almost without exception consists of mixtures of two or more crystalline phases. These phases may be distinguished magnetically by a number of parameters which are dependent on structure, composition and particle-size. Commonly these segregated phases are intimately intermingled, for they developed from pre-existing simpler phases which were stable only at a higher temperature. As a result, there may be strong interaction of the magnetic fields of the different phases on one another. The magnetic properties of the bulk samples are thus determined both by the properties of the individual phases and by the nature of the magnetic interactions among them. The degree to which the phases have become segregated and the size scale on which the intergrowth textures have developed depend, among other things, on composition and thermal history. Kawai *et al.*[4] have demonstrated that in Japanese effusive rocks, unmixing at low temperatures is a process requiring tens of millions of years, whereas, in contrast, low-temperature unmixing can be detected in as little as three days in a particular sample which was first held at 750° C. for three days and was then quenched to room temperature. As a result of unmixing, the magnetic properties of rocks change conspicuously. At elevated temperatures, the rate of homogenization of unmixed phases varies greatly among different samples; heat treatment at 650° C. for 15 min. is sufficient to cause gross changes in the phase structure and composition of the magnetic fraction of numerous rocks. This fact has been observed repeatedly in many laboratories and is abundantly documented, especially in the Japanese works.

Stott and Stacey ignore these facts, assuming that their experiments on natural samples which have been heat-treated 15 min. at 650° C. and then cooled over a period of several hours while under axial stress give realistic replicas of typical conditions in Nature. Clearly, this assumption is not safe, except possibly for the case of some young rocks which were cooled quickly; it does not permit generalizations, for example, about the possible role of magnetostriction in influencing the directions of residual magnetization of samples of a dolorite sill which cooled over a period of hundreds of years while under load, remained under a load that decreased over millions of years while magnetic phases were segregating from original simpler phases, and finally were brought to the laboratory for measurement.

We feel that this oversight by Stott and Stacey should be pointed out for, in our opinion, there are already too many instances where conclusions founded improperly have given the subject of palæomagnetism a questionable status.

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Borides and Silicides of the Platinum Metals

A great number of intermediate phases exist in the systems of boron with platinum metals[1] but very little information about these phases is available. X-ray crystallographic studies of platinum metal borides have been initiated at this Institute, and we have determined three new structure types (tentatively called Ru_7B_3, RhB and IrB_{1-2} types) which will be discussed briefly in this communication. We have found evidence that the 'Rh_2B' phase with *C*23 structure reported by Mooney and Welch[2] might really be Rh_2Si.

The alloys were prepared by melting mixtures of the elements (99·7–99·8 per cent pure) in an arc furnace. The crystal structures were determined with single-crystal methods, while the lattice parameters were obtained from powder photographs.

The Ru_7B_3 structure. This structure is hexagonal and was recently described in detail[3]. The space group is $P6_3mc$ with two formula units in the unit cell. Ru_7B_3 and Rh_7B_3 crystallize in this structure, which is especially interesting for its close similarity to the Cr_7C_3 structure[4].

The RhB structure. The most probable space group of this orthorhombic structure is *Cmcm*. The four

Table 1. CRYSTALLOGRAPHIC DATA OF SOME BORIDES AND SILICIDES OF THE PLATINUM METALS

Substance	Space group	Lattice parameters (A.)
Ru_7B_3	$P6_3mc$	$a = 7\cdot46_7$, $c = 4\cdot71_3$
Ru_7B_3	$P6_3mc$	$a = 7\cdot47_5$, $c = 4\cdot77_6$
RhB	*Cmcm*	$a = 3\cdot30_3$, $b = 5\cdot68_7$, $c = 4\cdot34_3$
PtB	*Cmcm*	$a = 3\cdot35_6$, $b = 5\cdot80_9$, $c = 4\cdot06_3$
IrB_{1-2}	$I4_1/amd$	$a = 2\cdot81$, $c = 10\cdot27$
Ru_2Si	*Pnma* (*C*23 type)	$a = 5\cdot27_9$, $b = 4\cdot00_5$, $c = 7\cdot41_8$
Rh_2Si	*Pnma* (*C*23 type)	$a = 5\cdot40_8$. $b = 3\cdot93_0$, $c = 7\cdot38_3$

rhodium atoms of the unit cell are situated in 4(*c*) with $y = 0\cdot167$. The boron atoms occupy the 4(*b*) position, which corresponds to octahedral holes in the metal skeleton. The final *R*-value of the 45 observed *0kl* reflexions was 8·9 per cent. PtB is isomorphous with RhB.

The IrB_{1-2} structure. In iridium–boron alloys around the equiatomic composition a phase with simple structure was observed. Since from structural reasons the ideal composition of this phase probably is IrB_2 it will be denoted IrB_{1-2}. The space group is $I4_1/amd$ with four iridium atoms in 4(*a*). With this arrangement of the metal atoms an *R*-value of 9 per cent was obtained for the thirty observed *h0l* reflexions with $\sin\theta/\lambda > 0\cdot8$. Eight boron atoms can be accommodated in 8(*e*) with $z \sim 0\cdot42$, but this position is probably only partly occupied. The boron atoms have the same environment as those in the AlB_2 structure.

Borides and silicides of the C23 *type.* We have found that intermediate phases of the *C*23 type exist in the Ru–Si and Rh–Si systems, but we could not confirm that 'Rh_2B' has this structure. It does not seem unlikely that the 'Rh_2B' crystals studied by Mooney and Welch[2] in reality had the composition Rh_2Si. We would like to put forward the following arguments to support this suggestion. (1) The ability of amorphous boron to reduce silica has been pointed out already by Moissan[5], and recently[6] it has been shown that nickel–boron samples easily react with silica to form Ni_6Si_2B. Thus, it is not unreasonable to assume that also rhodium–boron samples are able to react with silica to form alloys containing silicon. (2) The lattice parameters reported for Rh_2B ($a = 5\cdot42$ A., $b = 3\cdot98$ A., $c = 7\cdot44$ A.) are within experimental errors equal to (or slightly larger than) those of Rh_2Si (see Table 1). If 'Rh_2B' and Rh_2Si were isomorphous, one would expect the unit volume of the former to be smaller than that of the latter. (3) The experimental density of the 'Rh_2B' alloy of Mooney and Welch[2] was 10·5 gm./cm.^{3}, which agrees better with the calculated value for Rh_2Si (9·90 gm./cm.^{3}) than with that for 'Rh_2B' (8·96 gm./cm.^{3}). (4) The published intensity data for 'Rh_2B' are compatible with our suggestion. If the calculated *h0l* structure factors for Ru_2Si (which we have refined from single-crystal data) are compared with those observed from 'Rh_2B', an *R*-value of 0·21 is obtained, whereas the value of 0·26 was reported for 'Rh_2B'. (5) Finally, the average Rh–B distance in 'Rh_2B' is 2·50 A., which is much longer than one would expect for metal–boron contacts (in Ru_7B_3 the average *Me*–B distance is 2·16 A., in RhB 2·19 A.), whereas 2·50 A. is a very reasonable Rh–Si distance.

It is also possible that the reported Pd_3B_2 phase[1] might have been Pd_2Si (perhaps with dissolved boron), which crystallizes in the revised (hexagonal) *C*22 structure[6,7].

We wish to thank Prof. G. Hägg for his kind interest and the European Commission of Air Research and Development Command for financial support (Contract No. *AF*61(052)-40).

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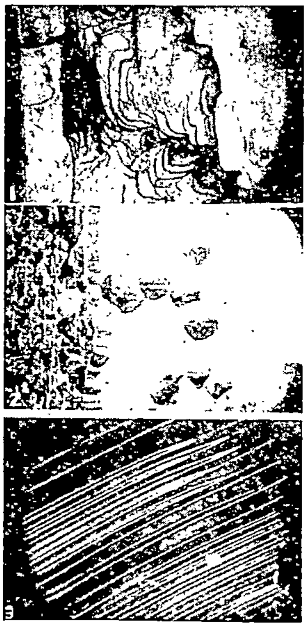
Slip Sources on Sodium Chloride Surfaces

MANY experiments have been carried out with sodium chloride crystals to investigate the Joffé effect, according to which the dissolution of surface layers by surrounding solvents results in an improvement of the plastic properties of the crystal. Hollomon and Fisher[1] suggested that this might be due to surface sources of slip which play an important part during the initiation of plastic flow.

Sodium chloride crystals were grown from a melt and their surfaces investigated with an opaque illuminator microscope. A set of small lines was observed. The crystals were then put in a not quite saturated aqueous solution of sodium chloride, which acted as an etching reagent. After a few minutes of etching the solution was made supersaturated by temperature regulation so that a slow growth started on the etched surface. A typical result is shown in Fig. 1. It is believed that the etching revealed slip sources which then became amplified by the subsequent epitaxy from the supersaturated solution. The curved lines may be parts of Frank–Read sources, which usually cover the surfaces of sodium chloride crystals grown from a melt[2]. On surfaces which do not contain slip sources the epitaxy reveals a cubic structure without curvature.



Figs. 1–3. (× 125)

Fig. 2 shows a specimen which was etched for a few minutes in 80 per cent alcohol. Etch pits became visible. On the left the surface is crowded with pits, on the right the pits are better resolved. As the pits are pointed they may be dislocations[3]. The left side seems to be the result of a crack passing slowly through the crystal. Such cracks are known to create a large number of dislocations at their edge.

If the crystals are heated to a high temperature (600° C.) and quenched, discontinuous lines become visible after etching. Fig. 3 shows a typical example on a dark field. It is suggested that the discontinuous lines consist of dislocations piled up against some obstacle.

If the surfaces are dissolved in water the number of observable slip sources is considerably reduced.

This work was carried out in the Institute for Experimental Physics of the University of Technology, Budapest. I wish to thank B. Jeszenszky for valuable discussions. A detailed paper will be published in *Acta Physica Hungarica*.

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Unpleasantness of Distorted Sounds : a Criterion derived from the Distortion Spectrum

For lack of any proved method of objective assessment the degree of non-linear distortion permissible in transmission systems which handle high-quality speech and music programmes has been decided, up to the present, entirely on the basis of long experience. While collecting data to support a more factual approach to this subject the following experiments have been made.

Pulses of pure tone, rather like staccato piano notes, have been distorted in various ways and the 'unpleasantness' of the resulting sounds have been compared, and an objective criterion, C_t, computed. This shows satisfactory correlation with the unpleasantness and can be defined as follows:

$$C_t = \sum_{2}^{n} n^2 (p_n - t); \quad (p_n - t) \text{ positive}$$

where n is harmonic number, p_n is percentage amplitude of nth harmonic and t that percentage of the signal (at its crest) which is just audible.

When the level of the crest of the pulse is 70 phons, and the sounds are presented under good listening conditions (for example, ambient noise in the region of 30 phons) a value of $t = 0{\cdot}2$ gives good correlation with subjective assessment. It is suggested that $t = 0{\cdot}5$–$1{\cdot}0$ may be more appropriate so far as domestic broadcasting is concerned. Since t is that harmonic percentage which is just audible, the value of t will fall below these figures if the signal/noise ratio is increased, or rise if the ratio is reduced.

The validity of the criterion C_t has been tested by setting up pairs of distortion spectra, which differ radically both in their general character and in their band-width, and adjusting one of the spectra until the two sounds are equally unpleasant. If the signal frequency lies in the range 250–1,500 c./s., the value of the criterion C_t derived from each spectrum will then be substantially the same, provided the appropriate value of t is adopted; anomalies occur outside this frequency-range.

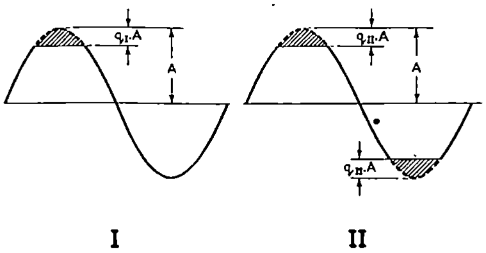

Fig. 1

A form of distortion which is easily adjusted and controlled is shown at I in Fig. 1; the proportion q_I of the amplitude, A, of the sine-wave can be varied by adjusting the steady bias applied to a diode shunting the signal path. The criterion C_t increases roughly as $\sqrt{q}$, when t is made very small or zero. Distortion of the type shown at II in Fig. 1 is often found, although in a form very considerably attenuated by negative feedback, in high-power (for example, 150 kW.) modulating-amplifiers for amplitude-modulated radio transmitters; in this case both positive- and negative-going parts of the wave are limited. The correlation between the criterion C_t and the unpleasantness of both types of distortion has been investigated, and a report will be published in due course elsewhere.

The outcome of one set of experiments is as follows: it is found that when $q_I = q_{II}$, and q is in the range $0{\cdot}5 > q > 0$ the signal I in the figure is (within the limits of experimental error) as unpleasant as the signal II (although there is a great difference in tone-colour). On comparing the spectra the two criteria are found to differ by less than 10 per cent when t is made zero and at least eight terms are summed.

Now when $q_I = q_{II}$ the spectrum of the signal II is similar to the spectrum of I, except that all the odd terms are doubled in amplitude and the even terms are entirely absent. Thus on summing the terms to derive the criterion, the absence of half of them is made up for by the doubled amplitude of those remaining.

It is important to notice that roughly the same effect would have been obtained if n or n^3 were substituted for n^2 in the equation; that the signals I and II sound equally unpleasant, therefore, provides no direct test of the criterion. However, it does demonstrate that any criterion (such as the total harmonic percentage) which is based upon the summation of terms in $(p_n)^2$, must necessarily fail to correlate with the unpleasantness.

There is some evidence that $\log(C_t)$ may be used to predict the 'rating' of the distortion; thus, if the rating-scale is expressed by a series of numbers such as: 1, 'distortion not perceptible'; 2, 'perceptible with effort'; 3, 'perceptible without effort' and so on, the rating number tends to vary with $\log(C_t)$.

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CHEMISTRY

Smoke Emission of Low-Temperature Chars

In a recent communication by Adams, Gaines, Gregory and Pitt[1], the authors make the usual assumption that coal contains a material of character such that it is partly removed, as tar, on heating. I wish to offer an alternative suggestion.

It is generally admitted that a great part of bitumin coal substance has a polymethylene structure.

It is a well-known fact that the early products of the carbonization of coal are ethane, ethylene, hydrogen, methane and tar.

Now in a series of papers summarized and extended by Dr. C. G. Silcocks and myself in two recent papers[2], we show that ethane and ethylene react at temperatures in the region in which low-temperature carbonization is usually effected, thus:

$$C_2H_4 + C_2H_6 = C_4H_8 + H_2 \qquad (1)$$

$$C_2H_4 + C_2H_4 = C_4H_8 \qquad (2)$$

The product, in the presence of excess hydrogen, is converted mainly into methane, and, in the absence of hydrogen, it loses hydrogen and polymerizes, forming tarry bodies. Of the nature of these strange bimolecular reactions I can only say that they appear to be homogeneous *in vitro*.

In a recent communication published in the *Journal of the Institute of Fuel* (April 1957) I suggested that this combination of reactions may account for the formation of methane and tar during the process of low-temperature carbonization of coal and, if this is the case, the formation of tar may continue so long as any methylene structure remains in the coal. *In vitro* the bimolecular reactions (1) and (2) appear to be homogeneous, but what may happen when C_2-hydrocarbon is formed from the methylene structure within the mass of the coal is unpredictable.

The bimolecular reactions (1) and (2) are unique in that propane and propylene behave in no way similarly. But during the pyrolysis of higher hydrocarbons, C_2-hydrocarbons are always formed; then further changes follow as indicated.

In 1938, I communicated to the Faraday Society a paper on the system:

$$\text{carbon} + \text{hydrogen} \rightleftharpoons \text{methane}$$

At temperatures below 700° C. the equilibrium relations appeared to indicate that methane was formed by a reaction represented by:

$$>CH_2 + H_2 \rightleftharpoons CH_4$$

The work was made difficult by the fact that equilibrium was established slowly, and leakage of hydrogen through the walls of the reaction vessel had to be allowed for. By itself I should not have paid much attention to this result, but it falls into line with the other experimental work I have mentioned.

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Effect of Carrier Gas on Katharometer Response

In recent communications[1] the relative effects of gases of high and low thermal conductivity on the response of katharometers to the presence of eluted substances have been considered. Several recent publications[2-5] have dealt with this, but a few points can usefully be emphasized.

The classical heat balance of a katharometer is given by[6]:

$$\frac{i^2R}{J} = Ctk_1 + H \qquad (1)$$

where i is the filament current, R its resistance, C a cell constant, k_1 the thermal conductivity of the gas, and t the difference in temperature between the wire and the walls of the cell. H represents the heat lost by a variety of means such as convection, conduction down the leads, radiation and transfer to a flowing gas. This has been passed over by Ray and by Schmauch and Dinerstein but is of great importance, and the last factor particularly is important in katharometer behaviour, as shown by Bohemen and Purnell[2].

The sensitivity of a katharometer is measured in electrical units. Thus, a change $\mathrm{d}t$ in the temperature of the wire produces a change $\mathrm{d}R$ in its resistance and hence a change in potential of $i\mathrm{d}R$ volts. Ignoring H, as above, it can then be shown[3] that:

$$(\mathrm{d}E)_t = \frac{J\alpha Ct^2}{i}\,\mathrm{d}k_1 \text{ (volts)} \qquad (2)$$

where $(\mathrm{d}E)_t$ is the katharometer response at t° C. and α is the temperature coefficient of resistance of the wire.

Whence, from (1):

$$(\mathrm{d}E)_t = \alpha . \frac{i^3R^2}{CJ{k_1}^2}\,\mathrm{d}k_1 \qquad (3)$$

However, also from (1) and (2):

$$(\mathrm{d}E)_t = \alpha\,\frac{(JRt^3)^{1/2}}{(Ck_1)^{1/2}}\,\mathrm{d}k_1 \qquad (4)$$

Equation 4, which has been verified experimentally[3], applies, of course, only to one carrier gas, but is interesting in that should equation 3 be generally true, as argued by Ray, the response of katharometers at constant temperature of the wire is inversely proportional to ${k_1}^{1/2}$, in contrast to the statements both of Ray and of Schmauch and Dinerstein. Furthermore, there is evidence[3] supporting equation 4 which fits the facts of hydrogen and helium systems remarkably well. However, this is purely fortuitous and due to the fact[1] that $\mathrm{d}k_1/\mathrm{d}x$ is approximately equal for these two gases. If the thermal conductivity (k_2) of a diluent is very much less than that of the carrier then $(k_1 - k_2)/k_1$ or $\mathrm{d}k_1/k_1$ should be approximately equal for two carriers. Whence the ratio of helium to hydrogen responses becomes:

$$\frac{(\mathrm{d}E)\mathrm{He}}{(\mathrm{d}E)\mathrm{H}} = \sqrt{\frac{k_1\mathrm{He}}{k_1\mathrm{H}}} \qquad (5)$$

a result which simply does not fit the facts. It has been found necessary to qualify the significance of $(k_1 - k_2)/k_1$ by the introduction of constants only approximately unity, thus: $(b_1k_1 - b_2k_2)/k_1$. I understand that there is theoretical justification for this (Littlewood, A. B., private communication). When considering other carrier gases the importance of H (equation 1) cannot be ignored as it can with hydrogen and helium. This greatly complicates the mathematics, and systems worth studying would be helium in hydrogen and water vapour in both, where k_1 and k_2 are nearly equal but H can be ignored.

A final point not mentioned by Ray is that the temperature of the wire rises when the working substances he uses are eluted in helium, but falls when they are eluted in argon. This has been missed by Schmauch and Dinerstein, who give responses only for substances which cause a rise in the temperatures of the wire with nitrogen. The results are not, therefore, comparable. In any event, the point is a simple one. Helium is obviously much more easily detected by katharometer in nitrogen or argon than in hydrogen.

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Use of Katharometers in Gas Chromatography

IN a recent communication[1], Ray attacks the tenet that "the use of hydrogen or helium as the carrier gas in gas chromatography gives the highest sensitivity with a thermal conductivity detector". He derives an equation describing katharometer behaviour from which he infers that the carrier gas with the lowest thermal conductivity will give the highest sensitivity. He concludes that nitrogen, argon, or carbon dioxide will provide greater sensitivity than hydrogen or helium. We wish to point out that the conclusion drawn from this equation does not follow generally, although it may be valid in certain instances. Furthermore, a basic assumption in Ray's derivation is contrary to the usual operating procedure for katharometers.

His equation, $dt/dx = -a(k_1 - k_2)/k_1^2$, states that the sensitivity of the detector, dt/dx, is proportional to the difference between the thermal conductivity of the carrier gas, k_1, and the vapour, k_2, and inversely proportional to the square of the thermal conductivity of the carrier gas. As Ray implies, this function has an arbitrarily large negative value as k_1 approaches zero. He fails to note that it also exhibits a maximum when the thermal conductivity of the carrier gas is twice that of the vapour being analysed.

We have computed values (Table 1) of katharometer sensitivity using this equation and the values of thermal conductivity for various carrier gases and organic vapours given in the International Critical Tables[2] for 0° C. It will be seen that argon provides high sensitivity for methane, low sensitivity for ethylene and again high sensitivity for benzene. This is because in the first instance the thermal conductivity of argon is approximately one-half that of the methane; in the second instance, the thermal conductivities of carrier and vapour are nearly identical, and in the third instance the thermal conductivity of argon is almost exactly twice that of benzene. Thus, the response of the katharometer may be either positive or negative depending on whether the organic vapour being detected has a smaller or larger thermal conductivity than the carrier, and also varies greatly in absolute value. In contrast, helium, the thermal conductivity of which is high relative to organic vapour, gives a nearly constant sensitivity, which permits quantitative estimation of the concentration of each component in a complex mixture.

Table 1. THERMAL DETECTOR SENSITIVITIES RELATIVE TO METHANE IN HELIUM

	Argon ($k = 1·58$)	Nitrogen ($k = 2·28$)	Helium ($k = 13·9$)
Methane ($k = 2·94$)	−9·82	−2·11	1·00
Ethane ($k = 1·80$)	−1·58	1·61	1·11
Ethylene ($k = 1·64$)	−0·44	2·11	1·12
m-Pentane ($k = 1·16$)	2·98	3·86	1·16
Benzene ($k = 0·825$)	5·44	4·91	1·19

Table 2. CONSTANT HOT-WIRE TEMPERATURE

	Argon	Nitrogen	Helium
Methane	−1·09	−0·35	1·00
Ethane	−0·18	+0·27	1·10
Ethylene	−0·05	0·35	1·12
m-Pentane	0·34	0·62	1·15
Benzene	0·59	0·81	1·19

It should also be noted that Ray's equation 1 implies that in all experiments the same current flows in the detector. However, it is common practice to increase the current when using a carrier gas of higher thermal conductivity, so that the difference in temperature between hot wire and cell wall is kept constant. Under these conditions the approximate equation will be $dt/dx = -a(k_2 - k_1)/k_1$.

Relative sensitivities (Table 2) have been computed for this mode of operation. It is clear that helium is eminently superior to either argon or nitrogen. Thus, while it may be true that the use of a carrier gas of thermal conductivity much lower than that of any organic component to be analysed would exceed helium in sensitivity, no gas now available is applicable to the large variety of substances at present being analysed by gas chromatography.

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Effect of the Carrier Gas on the Sensitivity of Thermal Conductivity Detectors in Gas Chromatography

IT has recently been suggested[1] that the use of argon or other carrier gases of low thermal conductivity will lead to increased sensitivity of thermal conductivity detectors used in gas chromatography. While this may be so in certain special cases, it is by no means a general effect, and it is the purpose of this communication to point out some of the many disadvantages of carrier gases of low thermal conductivity. The effects we wish to discuss may be illustrated qualitatively by the use of the approximate equation[1] for the variation of filament temperature (t) with composition (x) of the eluted gas.

$$\frac{dt}{dx} = \frac{a(k_1 - k_2)}{k_1^2} \quad (1)$$

where k_1,k_2 are the thermal conductivities of the carrier gas and organic vapour respectively. Substituting the thermal conductivity data from Table 1 in equation 1 leads to the predicted relative sensitivities shown in Table 1. The substances investigated, benzene, *n*-heptane, chloroform, carbon tetrachloride and methyl chloride, would appear from Table 1 to show a higher sensitivity with argon than with helium but ethanol would show a lower sensitivity, and methanol would show a peak reversal compared to ethanol. It should be pointed out that these estimates are only crude approximations since the initial temperature of the detector filament is unknown and is probably considerably higher than 100° C. for our apparatus in which the block temperature is 100° C.

Table 1. THERMAL CONDUCTIVITIES OF GASES AND VAPOURS AT 100° C. (REF. 2)

Substance	k cal. cm.$^{-1}$ sec.$^{-1}$ deg.$^{-1}$	$\frac{k_1 - k_2}{k_1^2} \times 10^2$	
		Helium	Argon
Helium	39·85	—	—
Argon	5·087	—	—
Chloroform	2·333	2·36	+10·64
Carbon tetrachloride	2·048	2·38	+11·74
Methyl chloride	3·841	2·27	+ 4·81
Ethanol	4·99	2·20	+ 0·41
Methanol	5·161	2·18	− 0·28

Ideally, comparison of sensitivities for different carrier gases should be made with constant filament temperature rather than constant current. Such a comparison would lead to different relative sensitivities and generally lower sensitivities for argon relative to helium than those obtained in our experiments. Unfortunately, our experimental arrangement did not allow measurements of potential across the filament and therefore comparisons were made with the same filament current. This does not, however, vitiate our qualitative conclusions.

A Perkin–Elmer *F* column containing 25 per cent by weight of stationary phase was used at 100° C. with a flow-rate of 100 cm.^{3}/min. and a constant filament current of 140 m.amp. Results were obtained with various mixtures using a 'Gow-Mac' four-filament type thermal-conductivity cell as shown in Table 2.

Table 2 shows that the relative responses for various substances are more nearly equal with helium than with argon as carrier. In the first four systems recorded, the mixtures contained equal volumes of the two components. The sign of deflexion is taken relative to the ethanol peak; thus we see that for three of the systems the peaks are in the same direction as ethanol in argon and in the remaining three the peaks are reversed in argon. In fact, the ethanol peak is reversed in argon relative to helium. Secondly, we see that for some mixtures the detector is less sensitive in argon.

Table 2

Mixture	Sensitivity ratio EtOH/x	
	Helium	Argon
MeOH + EtOH	+0·86	+0·63
EtAc + EtOH	+1·19	+9·00
CCl_4 + EtOH	+1·15	−1·11
$CHCl_3$ + EtOH	+1·69	−1·78
CH_3I + EtOH	+0·65	−0·57
CH_3Cl + EtOH	+4·45	+ 126

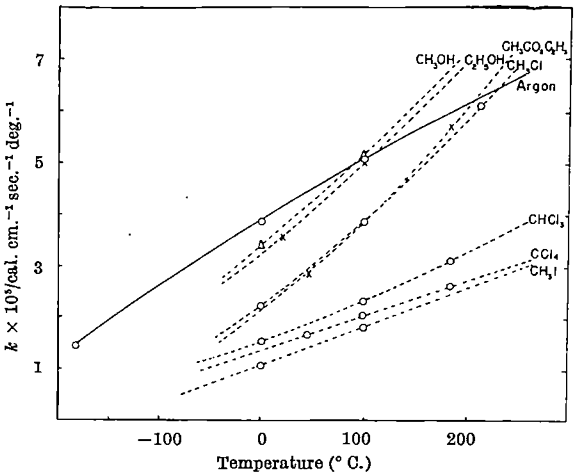

Fig. 1. Thermal conductivities of gases and vapours

If a vapour possessed the same thermal conductivity as the carrier gas at the effective temperature (which is not necessarily the filament or the block temperature), then the detector would be insensitive during the passage of eluted vapour through the conductivity cell. Such is almost the case with methyl chloride with a value of + 126 for the sensitivity ratio in argon shown in Table 2. This affords an approximate method of determining the effective temperature, which from Fig. 1 is around 260° C. Unfortunately there is no such obvious method of deducing the temperature with helium, although the temperature will be lower than in argon for any given current. Comparison with Fig. 1 shows that the sensitivity of systems exhibiting peak reversal in argon correlates with the distance from the argon thermal conductivity line.

The above results confirm the qualitative conclusions drawn from equation 1, that the variation of sensitivity when argon is used as carrier gas is large, varying from large positive sensitivities through zero to large negative sensitivities, whereas the sensitivity when helium is used as carrier gas is more nearly constant for a range of materials. Since gas chromatography is very often used to analyse for materials the nature of which is unknown and since the data on thermal conductivities are sparse, it would seem that helium or hydrogen is a better carrier gas to use for general purposes and that argon or other gases of low thermal conductivity should be used only in cases where calibration has shown that the ultimate sensitivity is substantially higher.

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Isotopic Composition of Boron and its Atomic Weight

After an extensive investigation, we conclude that a boron-11/boron-10 ratio of 4·00 (that is, 80/20) approaches the true natural abundance ratio much more closely than the presently 'accepted' value of 4·31 (81·17/18·83). The latter figure is based on a mass spectrometric investigation of boron trifluoride[1], a notoriously troublesome compound, in view of its adsorption characteristics resulting in instrumental 'memory'. Since publication of that work a number of attempts to verify the abundance ratio from boron trifluoride have resulted in a wide range of values.

On the other hand, abundance ratios calculated by various investigators from mass spectra of boron hydrides have been highly consistent, yielding ratios of approximately 4·00. Lest it be argued that this lower value may be peculiar to boron hydrides, we would like to point out that recent work in this laboratory with other compounds (for example, trimethylboroxine) has yielded the same ratio.

We therefore propose that in the future it would be far more reasonable to use the ratio 4·00 (80/20) to represent the natural isotopic abundance of boron. This would require in addition a revision of the atomic weight from 10·82 to 10·811, a change which seems well within the range of experimental error of earlier investigators[2].

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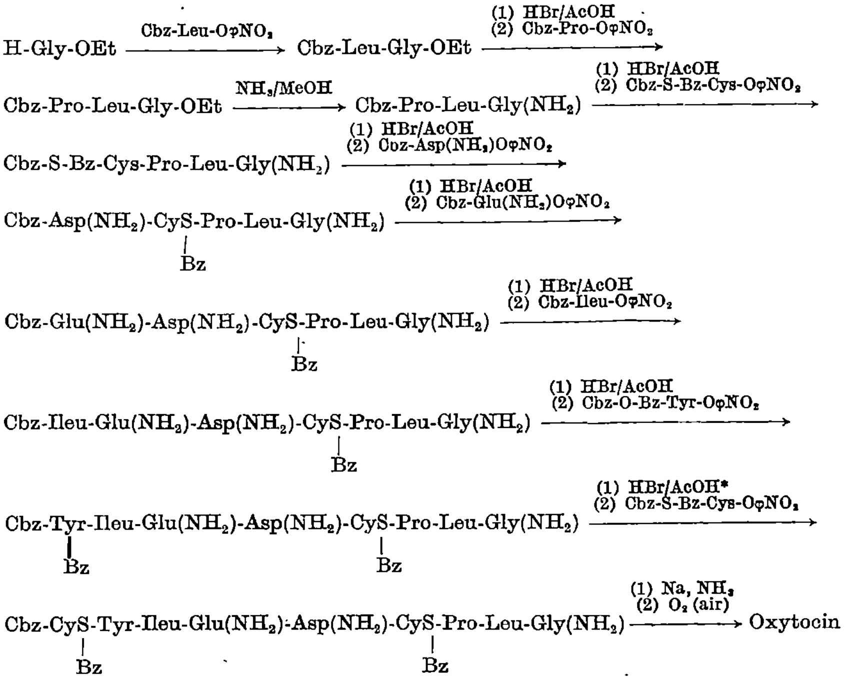
BIOCHEMISTRY

Synthesis of Oxytocin by the Nitrophenyl Ester Method

After the completion of work on the degration of oxytocin[1], this compound was synthesized in this laboratory[2]. Since that time several other synthetic methods leading to biologically active solutions of the crude hormone have been reported[3]. Recently, an improved synthesis of oxytocin was elaborated[4] by us. All these syntheses of oxytocin have the common feature of linking peptides together. It is well known, however, that formation of the peptide bond with a protected peptide as the acid component can lead to racemization[5], the extent of which depends on the components, the conditions and the method. No racemization was observed with the use of the azide method[6]. Nevertheless, the latter procedure can involve the formation of by-products other than diastereoisomers. To avoid racemization it is possible to take advantage of the protecting groups, for example, the carbobenzoxy group, which protects the amino-acid acylated by it not only against unwanted acylation but also against racemization. This protection is effective only if the carbobenzoxy group is joined to the amino-acid, the carboxyl group of which takes part in the peptide bond-forming reaction. Therefore it becomes necessary to start the synthesis with the C-terminal amino-acid, to link to it the next (protected) amino-acid, to remove the protecting group from the resulting dipeptide derivative, to couple to the free amino component thus formed the third (protected) amino-acid, etc. This manner of peptide-chain synthesis is practicable only if the method used for the formation of the peptide bond is unambiguous, leads to only one peptide, and gives high yields. All the mixed anhydride methods were eliminated as they usually



$$\text{H-Gly-OEt} \xrightarrow{\text{Cbz-Leu-O}\varphi\text{NO}_2} \text{Cbz-Leu-Gly-OEt} \xrightarrow[\text{(2) Cbz-Pro-O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-Pro-Leu-Gly-OEt} \xrightarrow{\text{NH}_3\text{/MeOH}} \text{Cbz-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-S-Bz-Cys-O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-S-Bz-Cys-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-Asp(NH}_2\text{)O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-Asp(NH}_2\text{)-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-Glu(NH}_2\text{)O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-Glu(NH}_2\text{)-Asp(NH}_2\text{)-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-Ileu-O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-Ileu-Glu(NH}_2\text{)-Asp(NH}_2\text{)-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-O-Bz-Tyr-O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH}}$$

$$\text{Cbz-}\underset{\substack{|\\ \text{Bz}}}{\text{Tyr}}\text{-Ileu-Glu(NH}_2\text{)-Asp(NH}_2\text{)-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) Cbz-S-Bz-Cys-O}\varphi\text{NO}_2]{\text{(1) HBr/AcOH*}}$$

$$\text{Cbz-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Tyr-Ileu-Glu(NH}_2\text{)-Asp(NH}_2\text{)-}\underset{\substack{|\\ \text{Bz}}}{\text{CyS}}\text{-Pro-Leu-Gly(NH}_2\text{)} \xrightarrow[\text{(2) O}_2\text{ (air)}]{\text{(1) Na, NH}_3} \text{Oxytocin}$$

* The O-benzyl group is removed from the tyrosine residue by hydrobromic acid in acetic acid. It is not necessary in the next step.

Fig. 1

lead to two acylation products, the separation of which, for example by crystallization, can be difficult, especially in cases of peptides with several amino-acids. After the elimination of many other unsuitable possibilities the nitrophenyl esters of acylamino-acids were found to be suitable for this purpose.

The use of acylamino-acid nitrophenyl esters in peptide synthesis was suggested and applied earlier by one of us (M. B.)[7]. An improved method for the preparation of such esters was proposed later by Schwyzer and his co-workers[8]. Recently, however, di*cyclo*hexylcarbodiimide was used by Elliot and Russel[9] for the esterification of acylamino-acids with *p*-nitrophenol and we have found this procedure to be very convenient, giving high yields of pure products. For the synthesis of oxytocin, the *p*-nitrophenyl esters of cbz-L-leucine, cbz-L-proline, S-benzyl-N-cbz-L-cysteine, cbz-L-asparagine, cbz-L-glutamine, cbz-L-*iso*leucine and O-benzyl-N-cbz-L-tyrosine were prepared. All these esters are stable, optically pure compounds with excellent crystallization properties. The synthesis of oxytocin with the aid of these esters is outlined in Fig. 1.

Lengthening the already existing chain by one amino-acid was achieved in very satisfactory yields, usually 90–100 per cent of the theoretical amount. The protected peptides were obtained in reasonable purity and gave good analyses even without further purification. Most of the intermediates were readily obtained in crystalline form. The purity of the protected nonapeptide is best demonstrated by the fact that on removal of the protecting groups by sodium in liquid ammonia, followed by aeration, oxytocin was formed in 78 per cent yield from it. Experimental details of this work will be presented elsewhere.

We believe that the method of synthesis outlined here may be useful both for structural proof and also for practical preparation of larger peptides of biological interest.

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Effect of Hydrolysis by Papain on the Combining Sites of an Antibody

PORTER[1] recently found that proteolysis of each of several different rabbit antiprotein antibodies with papain yielded three chromatographically separable fractions. Two of the fractions retained the capacity to combine with antigen, as shown by their ability to block specific precipitation, but would not form specific precipitates. The results indicated that the bivalent antibody molecule had in each case been split into two univalent fragments which retained specific activity and a third fragment lacking a combining site.

The use of anti-hapten antibody permits determinations of the specific binding of hapten, which provide a direct measure of the effect of a given treatment on the average equilibrium constant and the number of combining sites. In contrast with the precipitin reaction, quantitative measurements can be made with only one active site present on a molecule or fragment. With this technique we have found that hydrolysis of the antibody molecule by crystalline papain into fragments about one-third the original size has little effect on the capacity to bind hapten; that is, the combining sites in the degraded molecules are almost completely intact.

Experiments were done with a γ-globulin fraction of rabbit anti-*p*-azobenzoate antibody (containing 6·1 per cent of antibody specifically precipitable by an ovalbumin-*p*-azobenzoate test antigen[2]) and also with specifically purified antibody (73 per cent precipitable). Binding measurements were carried out by equilibrium dialysis with radioactive *p*-iodobenzoate having a radiochemical purity greater than 99 per cent. Methods used for the preparation of specifically purified antibody and for equilibrium dialysis have been described in detail[2,3].

Preparations of γ-globulins were made by the procedure of Kekwick[4] and were found to migrate as a single peak (6·5–7 S.) in the ultracentrifuge. Papain (twice crystallized) was purchased from the Worthington Company.

Antibody or normal γ-globulin preparations were treated at *p*H 7 with the amounts of papain and in the buffer indicated in Table 1. Mixtures were allowed to stand for 18–20 hr. at 37° C., then at room temperature. During the next 6 hr., measurements were made in the ultracentrifuge; equilibrium dialysis was then carried out with portions of the same samples.

Results are given in Table 1. For the samples treated with papain the $S_{20,w}$ values fall in a narrow range (3·4–3·6 S.) as compared with 6·5–7·0 S. for the untreated antibody γ-globulin or normal γ-globulin. None of the faster-moving material (6·5–7 S.) remained in any of the preparations treated with papain. In the case of antibody γ-globulin the amount of papain used was varied by a factor of 10. Thus the use of more enzyme resulted in little change in the apparent sedimentation constant, although the fraction of dialysable protein increased from 13 per cent (sample 4*A*) to 42 per cent (sample 6*A*). The $S_{20,w}$ values for the hydrolysed samples are in close agreement with those found by Porter[1], who observed a single peak with $S_{20,w} = 3{\cdot}5$, and a molecular weight of 55,000–60,000 (as compared with 160,000 for untreated antibody). The small amounts of papain ($S \simeq 2{\cdot}4$)[5] used did not appear in the sedimentation patterns as a separate peak.

Table 1. Effect of Crystalline Papain on Rabbit Anti-*p*-Azobenzoate Antibody*

Experiment No.	Sample	Papain used (mgm.)	$S_{20,w}$†	Conc. labelled *p*-iodobenzoate bound‡ ($M \times 10^{6}$)
1*A*	Normal γ-globulin	0	6·7	—
2*A*	Normal γ-globulin	16·5	3·4	0·06 ± 0·03
3*A*	Antibody γ-globulin	0	6·5	2·91 ± 0·07
4*A*	Antibody γ-globulin	1·7	3·6	2·66 ± 0·07
5*A*	Antibody γ-globulin	4·2	3·5	2·58 ± 0·03
6*A*	Antibody γ-globulin	16·5	3·5	2·17 ± 0·04
1*B*	Specifically purified antibody	0	7·0	5·07 ± 0·03
2*B*	Specifically purified antibody	0·5	3·5	4·75 ± 0·06

* Hydrolysis at 37° C. for 18–20 hr.; *p*H 7·0. Buffer contained sodium salts of phosphate (0·1 *M*), versene (0·002 *M*) and cysteine (0·01 *M*). 200 mgm. γ-globulin (series *A*) or 8 mgm. specifically purified antibody (series *B*) present in each mixture. Total volume 10 ml. in series *A*, 1·4 ml. in *B*. Papain added as an aqueous solution in two equal portions, at zero time and after 1½ hr.

† Sedimentation at 59,780 r.p.m. in 'Spinco' model *E* ultracentrifuge. Concentration of protein in sedimentation of series *A*, 10 mgm./ml. except for sample 1*A* (15 mgm./ml.); concentration in series *B*, 5·8 mgm./ml.

‡ Equilibrium dialysis in triplicate at 5·0 ± 0·1° C. with mean deviations shown. Free concentration of radioactive *p*-iodobenzoate after equilibration; in series *A*, $2·74 \times 10^{-6}$ *M*; in series *B*, $4·49 \times 10^{-6}$ *M*. Maximum deviation in free concentration in either series, 3 per cent.

In contrast with the large decrease in molecular size are the small changes in binding capacity. For samples 2*B* or 4*A*, which exhibited a single peak at 3·5 or 3·6 S., the concentration of hapten bound was more than 90 per cent as large as that for the corresponding untreated antibody preparation at the same free hapten concentration. Since the free hapten concentration was held constant, the results indicate that the decrease in the average binding constant or in the total number of binding sites was less than 10 per cent[6]. The use of larger amounts of papain resulted in somewhat greater decreases in binding capacity (up to 25 per cent) but most of the combining sites were evidently still intact.

Treatment with papain resulted in each case in complete loss of ability to precipitate with the ovalbumin–*p*-azobenzoate test antigen, as shown by tests made with a wide range of antigen concentrations. Control experiments, in which the papain was inactivated by treatment with 0·01 *M* ferricyanide prior to addition of antigen, showed that this failure to precipitate was due to the action of papain on the antibody (rather than on the antigen).

The results indicate that the rabbit antibody molecule can be degraded to a non-precipitating form of relatively low molecular weight with little effect on the specific combining sites. It appears also that measurements of binding capacity provide a convenient quantitative method for investigating the properties of these apparently univalent antibody fragments.

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Regeneration of Cellulose Acetate Membranes used for Zone Electrophoresis

The method described by Kohn[1] for the analysis of serum proteins by zone electrophoresis on strips of cellulose acetate membrane has been proved to be of great value. The development of this technique, as a micro-electrophoretic method[2], has emphasized the importance of cellulose acetate as a stabilizing medium. The sheets of cellulose acetate are relatively expensive compared with filter paper, and their higher cost may deter workers from using this excellent material. It has been found that the cellulose acetate membrane strip may be used several times after suitable treatment by the method to be described.

On completion of an analysis the used strip of cellulose acetate membrane with the stained bands of protein is placed in a shallow dish containing 200 ml. of buffer at *p*H 8·6 (veronal, sodium bicarbonate or sodium borate, ionic strength 0·05–0·1) to which is added 2·0–4·0 ml. trypsin solution. The trypsin solution contains 64 units of trypsin per ml. and is standardized by the method described by Coles[3]. The digestion of the protein occurs rapidly for quantities of protein in the range 100–200 μgm. and is complete at 37–39° C. in 2 hr.; but the digestion of 700 μgm. of protein, used with longer and wider strips, is not complete in 2 hr. and sometimes required periods of 16 hr. The longer digestion period is necessary to regenerate strips of cellulose acetate membrane which have been stored in a dry condition for some months after staining. After digestion of the protein, the cellulose acetate membrane strip is washed with distilled water and re-equilibrated in the buffer solution used for the electrophoretic separation. It is then ready for further use.

The cellulose acetate is quite stable under the conditions of regeneration: and in one instance a membrane strip has been regenerated four times without any apparent deterioration; this strip was dyed with lysamine green, bromphenol blue, nigrosine and finally bromphenol blue again for its use on the first, second, third and fourth occasions respectively.

In one instance 700 μgm. of serum protein had been separated into its component fractions by electrophoresis on a cellulose acetate membrane in a buffer solution to which copper sulphate had been added. The regeneration process, performed several months after the membrane had been dried, was not complete. The globulin fractions were digested by the trypsin; but the large stain corresponding to the albumin fraction was not removed. In this case, after treatment with trypsin, the membrane was washed with distilled water, then twice with ethyl alcohol and was finally equilibrated against benzene. The membrane appeared translucent and all traces of dye disappeared. The membrane was then washed with ethyl alcohol, followed by distilled water and finally re-equilibrated against the buffer solution unchanged. Its performance in use after regeneration was quite normal, and another sample of normal serum protein was fractionated successfully.

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Amperometric Determination of Sulphydryl Content of Blood and Tissues

THE total, non-protein and protein sulphydryl contents of biological materials can be determined by using two different analytical procedures: one for the determination of total sulphydryl (protein sulphydryl + non-protein sulphydryl) values and the other for the determination of non-protein sulphydryl values. The protein sulphydryl values are obtained by subtracting the non-protein sulphydryl values from the protein sulphydryl values. Most of the available methods, however, are often complicated, time-consuming and more or less non-specific. In an earlier communication[1] it was reported from this laboratory that, with a little modification, the amperometric method of Benesch, Lardy and Benesch[2] can be used for the specific determination of the total sulphydryl content of biological materials. It has since been observed that the method can be adapted for the non-protein sulphydryl determinations in the same materials. Thus it is possible to use a simple, specific and rapid method for the determination of all the three sulphydryl fractions in biological materials.

Table 1. CONCENTRATION OF TOTAL, NON-PROTEIN AND PROTEIN SULPHYDRYL IN RAT BLOOD AND TISSUES

The means of results with number of determinations in parentheses are given. The results are expressed in mgm./100 gm. for wet tissues and mgm./100 ml. for blood

Sample analysed	Total sulphydryl	Non-protein sulphydryl	Protein sulphydryl*
Whole blood	91·4 (8) 83·6–100·0	2·9 (4) 2·5–3·3	88·5
Liver	55·4 (7) 51·4–58·8	26·4 (4) 23·4–32·0	29·0
Kidney	48·3 (3) 45·0–53·0	11·3 (4) 8·7–13·1	37·0
Heart	31·2 (3) 28·0–33·0	7·2 (4) 6·8–7·9	24·0
Pancreas	25·4 (6) 20·0–30·4	6·7 (4) 6·5–6·9	18·7

* These values were obtained by subtracting the means of non-protein sulphydryl values from the means of total sulphydryl values.

The amperometric titration apparatus, with the exception of the platinum electrode, is assembled according to Benesch, Lardy and Benesch. For the construction of the platinum electrode, four strands (each 35 mm. long and 0·5 mm. diam.) of tightly twisted platinum wires are sealed in a soft-glass tubing in such a way that 15–20 mm. of the bare metal protrudes beyond the glass. The projecting wires are bent laterally into a U-shape. This electrode, in contrast to that used by others[2], greatly increases the sensitivity of the apparatus. For total sulphydryl determinations tissue homogenates and hæmolysed blood samples[1] are used. For non-protein sulphydryl determinations, sulphosalicylic acid (2·5 per cent solution) extracts of blood and tissues prepared according to the method of Benesch and Benesch[3] are used. Tissue homogenates (1–2 ml.), whole blood (0·1 ml. hæmolysed with 1 ml. of de-ionized distilled water), and sulphosalicylic acid extracts (1–5 ml.) of blood and tissues are titrated with 0·002 *M* silver nitrate in *tris* (hydroxymethyl) aminomethane buffer[2], *p*H 7·4. Each increment (0·1–0·2 ml.) of silver nitrate is added at 1-min. intervals and the micro-ammeter reading is taken at 55 sec. after each addition. It is essential to neutralize the sulphosalicylic acid extracts before addition to the buffer. The neutralization is carried out with 0·8 *M* sodium bicarbonate, the amount being determined in a separate titration using methyl orange as an indicator. During the titration of tissue homogenates pieces of connective tissue may adhere to the platinum electrode and cause mechanical interference with current readings. This is easily eliminated by first rotating the electrode for a few minutes in the buffer containing the homogenate (before the addition of silver nitrate) and then removing the adhering pieces from the electrode. To increase the specificity of the method a 'blank' titration is carried out with each estimation, using an excess of a 0·001 *M* solution of *p*-chloromercuribenzoate in 0·05 *N* sodium hydroxide. The technique of the 'blank' titration is very similar to those used by other workers[4,5]. Where x ml. of 0·002 *M* silver nitrate is required for a titration, $2x + 0{\cdot}1$ ml. of 0·001 *M* *p*-chloromercuribenzoate solution is added to block the sulphydryl groups. *p*-Chloromercuribenzoate is allowed to react for 5 min. before the titration. The final volume of the titration mixture, including the *p*-chloromercuribenzoate solution, is kept at 30 ml. Calculation: 1 ml. of 0·002 *M* silver nitrate ≡ 0·066 mgm. of sulphydryl.

The results of sulphydryl determinations, using the above method, in blood and tissues of rats (200–350 gm., both male and female) are summarized in Table 1.

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Selenite as a Relatively Weak Inhibitor of some Sulphydryl Enzymes

CONTINUING our studies on the oxidation of sulphydryl compounds[1], we found that selenite was a very active catalyst for the oxidation of cysteine, glutathione, dihydrolipoic acid, and coenzyme *A*. For the oxidation of glutathione, selenite was a far better catalyst than cupric chloride, the most active catalyst known previously[2]. Selenite is poisonous to animals but it is also claimed that selenium is an essential element. Selenium poisoning is an important unsolved problem: the toxic symptoms are complex and the mechanism of the poisoning is still obscure. Some investigators[3,4] believe that selenium compounds exert their toxic effect through interference with certain enzyme systems in the living organism, particularly through mercaptide formation with sulphydryl enzymes. However, most studies on enzyme inactivation had been done with tissue homogenates or yeast cells; and further information on the reaction of selenium salts with purified enzymes seemed desirable. The present communication reports the results of a study of the comparative inhibition of six well-known sulphydryl enzymes by selenite, cupric chloride, and *p*-chloromercuribenzoate.

Table 1. INHIBITION OF SULPHYDRYL ENZYMES

Inhibitor	Concentration (M)	Inhibition (per cent)					
		Alcohol dehydrogenase	Aldolase	D-amino-acid oxidase	β-Amylase	Lactic dehydrogenase	Urease
Selenite	0·01	48	29	—	—	—	—
	0·001	3	1	60	62	0	49
	0·0001	0	0	54	40	0	6
Cupric chloride	0·001	100	100	100	91	100	89
	0·0001	100	98	44	57	99	10
	0·00001	75	2	—	—	0	—
p-Chloromercuribenzoate	0·001	100	100	100	100	100	100
	0·0001	100	50	66	91	100	96

Yeast alcohol dehydrogenase (2× crystallized), muscle aldolase (5× crystallized), and kidney D-amino-acid oxidase were purchased from the Worthington Biochemical Corp.; muscle lactic dehydrogenase (crystallized) and urease (type V, special purity) from Sigma Chemical Co.; and barley β-amylase from Nutritional Biochemicals Corp.

The activities of alcohol dehydrogenase, aldolase, D-amino-acid oxidase, lactic dehydrogenase, urease, and β-amylase were measured by the methods of Racker[5], Swenson and Boyer[6], Frisell and Hellerman[7], Mehler *et al.*[8], Krebs and Henseleit[9], and Bernfeld[10], respectively. For the inhibition tests, the enzyme was incubated at room temperature with the inhibitor for at least 30 min. before determination of the activity.

The results in Table 1 show that, as compared with cupric chloride and p-chloromercuribenzoate, selenite is a rather weak inhibitor for the enzymes studied.

Lethal doses of selenite for several mammalian species are in the range of 1–15 mgm./kgm. body-weight[3]. In view of the fact that selenite is toxic in such small quantities, it does not seem possible that the effect is the result of mercaptide formation with sulphydryl compounds, such as glutathione and sulphydryl enzymes, *in vivo*. Also, from the results of our present studies, it appears unlikely that selenium toxicity is a result of direct inhibition of enzymes. It is more likely that the toxicity may be explained by the selenium-catalysed oxidation of such co-factors as glutathione, coenzyme A, and dihydrolipoic acid, and the resulting disturbances in intermediary metabolism.

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Labelled Keto-Acids in Duck Blood incubated *in vitro* with $NaH^{14}CO_3$

THE ability of duck blood rich in reticulocytes to incorporate *in vitro* carbon-14 from $NaH^{14}CO_3$ has been previously investigated[1]. Separately we have demonstrated incorporation into globin, hæm and stroma. The widespread incorporation suggested that the first products of carboxylation belonged to a pool from which all the substances we examined would be synthesized. This communication is concerned with an attempt to identify some labelled precursors (pyruvic and α-ketoglutaric acids).

45 ml. of duck blood were incubated for 18 hr. as previously described[1]. The plasma was separated from red cells by centrifuging. The plasma proteins were precipitated with 5 per cent metaphosphoric acid (4 ml. for 1 ml. of plasma) and discarded. The keto-acids were isolated from the supernatant as 2 : 4-dinitrophenylhydrazones[2], which were separated by paper chromatography (Whatman No. 1; *iso*-butanol, ammonia, 95 per cent ethyl alcohol, 70 : 20 : 10, v/v/v).

The 2 : 4-dinitrophenylhydrazones of pyruvic and α-ketoglutaric acids and an unidentified substance (R_F, 0) were eluted from the paper with 2 N sodium hydroxide. The eluate was acidified with hydrochloric acid and extracted with ethyl ether. After evaporation of the ether, the substances extracted were assayed for radioactivity by the method previously described[3].

In Table 1 the R_F of 2 : 4-phenylhydrazones of pyruvic and α-ketoglutaric acids and the specific activities of pyruvic and α-ketoglutaric acids are shown. The specific activity of the unidentified substance was 7,500 disintegrations/min./mgm. carbon. No attempt has yet been made to identify it.

Table 1

Material	Pyruvic acid	α-Ketoglutaric acid
Specific activity (dis./min./mgm. C)	1,820 ± 40	1,790 ± 50
R_F of 2 : 4-dinitrophenylhydrazone	0·38 (isomer 1) 0·58 (isomer 2)	0·13

The presence of labelled α-ketoglutaric acid seems to suggest that the Krebs cycle is effective in carbon dioxide fixation by duck blood *in vitro*. The labelled pyruvic acid also seems to be formed from the Krebs cycle acids (that is, oxalacetic acid). Moreover, labelled pyruvic acid could be formed via another pathway:

$$\begin{aligned}
&\text{ribulose-5-phosphate} \xrightarrow{CO_2} \text{6-phosphogluconate}\\
&\text{6-phosphogluconate} \longrightarrow \text{glucose-6-phosphate}\\
&\text{glucose-6-phosphate} \longrightarrow \text{2 pyruvic acid}
\end{aligned}$$

The incorporation of carbon dioxide by certain normal and tumour cells (but not by rabbit erythrocytes) in ribulose-5-phosphate was demonstrated by Baron *et al.*[4].

As succinic acid is formed via α-ketoglutaric acid in the Krebs cycle, and because succinic acid is a precursor of hæm[5], the hæm should also be labelled after incubation *in vitro* of duck blood with $NaH^{14}CO_3$.

Experiments in progress suggest that only part of the carbon-14 activity found in globin is due to amino-acids formed by transamination from α-ketoglutaric, oxalacetic and pyruvic acids. Indeed, arginine is also labelled.

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Purification of a Toxic Phytohæmagglutinin from Black Beans (*Phaseolus vulgaris*)

Beans, like other seeds of the Leguminosae, contain some proteins of remarkable biological activity. For many years a bean phytohæmagglutinin has been known[1,2]. Rigas and Osgood[3] recently described two different factors with hæmagglutinating properties. Other authors[4,5] have observed toxic effects in animals fed with raw beans or with certain preparations obtained by extracting bean meal. The hæmagglutinin factors prepared according to the original method[3] do not seem to be responsible for the toxic effect of raw beans, as they have only slightly toxic properties. Experiments carried out by one of us (W. J.) have also established the toxicity of beans that cannot be ascribed to the trypsin inhibitor (another protein) described by Bowman[6]. We therefore undertook to isolate the toxic components of beans in order to obtain further information about their properties.

Finely ground black beans (*Phaseolus vulgaris*) are extracted with 5 parts (w/v) of a solution of 1 per cent sodium chloride. By dialysing the filtered extract against water a large amount of inactive material is precipitated. Almost the whole activity is obtained by saturating the supernatant solution with ammonium sulphate. Different active fractions are prepared by saturating fractionally the redissolved precipitate with the same salt.

The main active fraction is obtained by precipitation between 55 and 70 per cent saturation of the redissolved, dialysed crude precipitate which has been previously adjusted to *p*H 6·0. After the precipitating and redissolving procedures have been repeated three times a highly purified protein is obtained which proves to be at least 90 per cent pure as revealed by electrophoresis and ultracentrifugation. The electrophoretic mobility, determined with the 'Spinco' apparatus model *H*, is $8·89 \times 10^{-5}$ cm.²/volt/sec. for a 0·9 per cent solution in barbiturate buffer of *p*H 8·6 and ionic strength 0·1. The isoelectric point should lie between *p*H 4 and 5. The sedimentation constant S_{20} for a 0·6 per cent solution in the same buffer was $5·9 \times 10^{-13}$ ('Spinco' ultracentrifuge model *E*). The protein, for which we propose the name 'phaseolotoxin *A*', is soluble in water, in 1 per cent sodium chloride solution and is precipitated by 30 per cent cold alcohol. It contains 13·5 per cent nitrogen (Kjeldahl) and 5·0 per cent reducing groups as determined by a modified Somogyi–Nelson method and calculated for glucose. These values relate to air-dried preparations.

Table 1. Physical and Biological Properties of Bean Fractions

Fraction	Electrophoretical mobility (cm.²/V./sec. × 10⁵)	Sedimentation constant ($S_{20} \times 10^{13}$)	Agglutinating activity (*c*) (μgm./ml.)	Toxic activity :	
				Dose (mgm./kgm.)	Mortality (*d*)
Phaseolotoxin *A*	8·89 (*a*)	5·9 (*a*)	3·0	50 60 100	15/2 6/5 9/9
Phaseolotoxin *A* after treatment by stroma	—	—	∞	100	4/0
Phaseolotoxin *A* heated to 80° C.	—	—	6·0	125	7/3
Fraction *B*	24·5 (*a*) 28·5 (*a*) 1·04 (*a*) 4·35 (*b*) 5·79 (*b*)	2·3 (*a*) 6·6 (*a*) 9·7 (*a*) 2·3 (*b*) 6·5 (*b*) 10·6 (*b*) 18·0 (*b*)	4·0	150 200	5/2 5/3

(*a*) Barbiturate buffer, *p*H 8·6; μ 0·1. (*b*) Phosphate buffer, *p*H 6·5; μ 0·1. (*c*) Minimum amount of toxin which gives positive results. (*d*) Toxin in mgm./kgm. mouse: number of animals used for the experiment/number of animals which died after injection.

Saturating the supernatant solution obtained after separating phaseolotoxin *A* by filtration yields another active fraction. The yield of this so-called 'fraction *B*' is low and not uniform. Even when precipitated three times it consists of three main components, as revealed by electrophoretic and centrifugation experiments. Among these no compound with the physical properties of phaseolotoxin *A* could be found.

The hæmagglutinating activity was determined with 0·25 per cent suspensions of washed sheep or mice erythrocytes in saline. 1·0 ml. of this suspension is mixed with 1·0 ml. of the active preparations obtained from beans in adequate dilutions and incubated at 37° C. for 30 min. and then centrifuged at 2,500 r.p.m. in a common laboratory centrifuge. The agglutination test is positive when the erythrocytes are not suspended by shaking.

Toxicity was studied in adult white mice after intraperitoneal injection of adequate dilutions of the preparations. The results of these experiments are shown in Table 1.

There are striking differences between phaseolotoxin *A* and the fraction *B*. These fractions have about the same agglutinating activity, but fraction *B* is at least three times less toxic. Therefore it may be assumed that black beans contain more than one toxic compound. Fraction *B*, different from phaseolotoxin *A* in its physical properties, also shows biological differences, and because of its relatively low toxicity and physical properties it resembles more the phytohæmagglutinin described by Rigas and Osgood[3].

Phaseolotoxin *A* proved to be a single component as revealed by the physical investigations, and these results suggest that hæmagglutinating and toxic properties are due to the same protein. This suggestion is strengthened by two other experiments. When a solution of 50 mgm. of the toxin is incubated for 30 min. at 37° C. with a suspension of 100 mgm. of human erythrocyte stroma in saline[7] the toxin is completely absorbed and after centrifugation the supernatant contains neither agglutinating nor toxic activity. Moreover, when a saline solution of phaseolotoxin *A* in a concentration of 25 mgm./ml. is heated to 80° C. for 60 min. the activities are not completely destroyed, although the solution becomes milkily turbid due to partial denaturation and precipitation. Hæmagglutinating and toxic activity, however, are reduced to the same extent, namely, to about 50 per cent. Boiling for 30 min. uniformly abolishes both activities completely.

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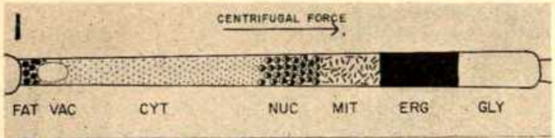
CELL PHYSIOLOGY

Nuclear Origin of Ribonucleic Acid

LIVING hyphæ of *Neurospora crassa* were centrifuged and their contents stratified in distinct layers. Starting at the centrifugal end, the layers were as follows (Fig. 1): glycogen, ergastoplasm (microsomes), mitochondria, nuclei, 'supernatant' cytoplasm, vacuoles and fat. Each fraction could be identified by cytochemical reactions. It was found that most of the cytoplasmic ribonucleic acid resided in ergastoplasm, some in mitochondria, and none was detectable in the 'supernatant'. Nuclei were relatively poor in ribonucleic acid.



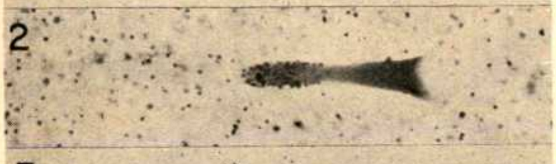


Fig. 1. Schematic presentation of a centrifuged hypha of *Neurospora*. *FAT*, fat; *VAC*, vacuole; *CYT*, 'supernatant' cytoplasm; *NUC*, nuclei; *MIT*, mitochondria; *ERG*, ergastoplasm (microsomes); *GLY*, glycogen. Centrifugal direction is to the right in all figures

Fig. 2. Autoradiograph of a centrifuged hypha fed tritiated uridine for 1 min. prior to centrifugation, stained with hæmalum. β-tracks in the nuclear layer; deeply stained layer, free of tracks, is ergastoplasm; glycogen and 'supernatant' not stained

Fig. 3. Autoradiograph of a centrifuged hypha fed tritiated uridine for 1 min. and unlabelled uridine for 1 hr., prior to centrifugation. β-tracks densest in ergastoplasm, less dense in nuclei and mitochondria; no significant increase of tracks over background in glycogen and 'supernatant'

The fact that nuclei became clearly separated from the cytoplasmic ribonucleic acid enabled us to localize the site of formation of ribonucleic acid. Mycelium, in its active growth phase, was fed tritiated uridine (uridine-5,6-^{3}H, 640 mc. per m.mole, 100 μgm./ml.) for given times, centrifuged and fixed. The mycelium was then washed in cold 5 per cent trichloracetic acid so that only nucleosides which were incorporated into ribonucleic acid remained. The preparation was mounted on a slide and covered with photographic emulsion[1]. After exposure and development, the autoradiographs showed tracks of β-decay at the sites of uptake of the precursor.

At short feeding times, from 1 to 4 min., the label appeared only in the nuclear fraction (Fig. 2). After 4 min., more and more label was found in cytoplasmic ribonucleic acid. In 1 hr., ergastoplasm was labelled much more heavily than the nuclei (Fig. 3), and some activity was found also in mitochondria, while the 'supernatant' remained virtually inactive. In brief, the distribution of the label became roughly proportional to the relative content of ribonucleic acid in the different fractions. When tritiated uridine was fed for 1 min. only and then washed out and replaced with an excess of non-labelled uridine, the label again appeared first in nuclei, to appear in the ergastoplasm only after several minutes. The labelling of ergastoplasm increased with time at the expense of nuclear label.

These results demonstrate that all the cellular ribonucleic acid is formed in nuclei and that it migrates into the cytoplasm later. Previous work of several investigators indicated that ribonucleic acid originated in nuclei[2] and the present experiments substantiate this hypothesis. These findings suggest that ribonucleic acid is a direct product of gene action. Ribonucleic acid is formed in nuclei, the seat of chromosomes and genes; it migrates into the cytoplasm; and it is required for the synthesis of proteins. A detailed report of this investigation will be published elsewhere.

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Hæmoglobin and 'Apparent Protein' in the Human Red Cell

THE concentration C_{Hb} of hæmoglobin is conventionally measured by dividing the hæmoglobin in gm. per cent by the fractional concentration ρ, allowance being made for incomplete packing in the hæmatocrit tube. If a high-speed hæmatocrit is used, ρ can be found with an error of about ± 1 per cent, and the hæmoglobin concentration can be measured by the cyanmethæmoglobin method with an error of about the same magnitude.

An independent method measures the concentration C_i in gm. per cent of what can be called 'apparent protein'; this includes hæmoglobin, colourless hæmoglobin precursors, lipoproteins, and 'stromatin'. Other substances contribute to a very small extent. The measurements of C_i are made with an *AO*-Baker interference microscope and with monochromatic green light, the red cells being turned into spheres by being suspended in a non-hæmolytic lecithin (Polanyi, personal communication). The equations are (Barer[1])

$$\mu = \frac{\theta\lambda}{360\,t} + n$$

and

$$C = \frac{\mu - n}{\alpha}$$

where θ is the phase retardation in degrees, λ the wave-length in the same dimensions as t, the cell thickness (equal to the diameter) of the spherical red cell, n the refractive index of the medium surrounding the cell, and α a constant called the specific refractive increment. Because the concentration of hæmoglobin in the red cell is so high, α has to be determined experimentally with a calibrated Nichols refractometer[2]. The calibration can be made with water ($n = 1{\cdot}333$), acetone ($n = 1{\cdot}3592$), and n-butyl alcohol ($n = 1{\cdot}3991$), all at 20° C.

About 1 ml. of normal or hypochromic blood is packed at high centrifugal force ($2 \times 10^4 g$), the supernatant column of plasma is removed, and the cells in the red cell column are hæmolysed by freezing and thawing several times; the hæmolysed sample is then spun in a high-speed centrifuge in order to free it as much as possible from ghosts, etc. The almost ghost-free supernatant column is removed, and its hæmoglobin concentration is found by the cyanmethæmoglobin method. Its refractive index is found with the Nichols refractometer by reference to the calibration curve. A graph is prepared in which refractive index is plotted against hæmoglobin concentration, straight lines being drawn for refractive index increments of 0·0020, 0·0018, etc. A vertical line is drawn through the determined hæmoglobin concentration, and a horizontal line is drawn through the determined refractive index. These two lines intersect at a point which corresponds to a value of the refractive index increment α. If the same experiment is repeated by determining the refractive index of the sample diluted with water in powers of 2, it is clear that the specific refractive increment is virtually constant with increasing hæmoglobin concentration, being essentially the same ($\alpha = 0{\cdot}0019 \pm 0{\cdot}0002$) when the hæmoglobin is dilute as when it is as concentrated as 30 per cent. It is a pleasure to thank Dr. H. G. Davies for telling me that this value of α is correct in his experience.

The mean value of C_{Hb} in normal males is $30{\cdot}1 \pm 0{\cdot}32$ gm. per cent. The value of C_i found by the refractometer is 33·28 gm. per cent in normal males, that is, about 10 per cent greater if C_{Hb} is considered as 100. It is inconceivable that this amount of 'apparent protein, not hæmoglobin' could be held in a surface ultrastructure of a thickness such as has been proposed, for, if it were, the ultrastructure, *dry*, would have to be about 1000 A. thick. No such value has been suggested, and so at least two-thirds of the 'apparent protein, not hæmoglobin' would have to be distributed in the red cell interior. Nothing can be said as to how it is distributed, except that if it were distributed uniformly, its concentration would be about 7 per cent of the hæmoglobin concentration.

In the case of persons with a hæmoglobin concentration of about 25 gm. per cent, the average discrepancy between C_i and C_{Hb} is about 16 per cent, C_{Hb} being again put at 100 gm. per cent. Over the range $C_{\mathrm{Hb}} = 25$–35 gm. per cent, the refractive index increment α is substantially constant.

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ANIMAL PHYSIOLOGY

Detection of Heterozygous Carriers in Glycogen Storage Disease of the Liver (von Gierke's Disease)

IN 1929, von Gierke[1] described a rare congenital disorder of carbohydrate metabolism characterized by excessive deposition of glycogen in various organs of the body. Cori and Cori[2] have shown that there is a deficiency of glucose-6-phosphatase activity in the liver in such patients. The occurrence of this condition in siblings[3] and among the offsprings of consanguineous matings[4], together with its equal distribution in both sexes, suggests that it is probably transmitted by a single autosomal recessive gene. In this situation, one would expect the disease to occur only in persons who receive two of the abnormal genes, one from each parent. If an individual is heterozygous for the condition, he will usually be free of clinical symptoms. Careful biochemical studies, however, might reveal minor departures from the norm[5].

Kapila, Kaul and Chattesjee[6] have reported on a family where the father, mother and siblings of a patient with von Gierke's disease showed a borderline response of blood glucose-levels to 0·25 ml. of adrenalin intramuscularly. One of the siblings also showed a flat oral glucose tolerance curve.

Recently, Wagner, Meyerriecks and Sparaco[7] have shown that there is an excessive accumulation of phosphorylated intermediates of the glycolytic cycle in the whole blood and plasma of patients with von Gierke's disease. Similar changes have now been noted among the parents of such patients and forms the basis of the present communication.

Glucose-6-phosphate and fructose-6-phosphate were determined in the following manner: 3–4 ml. of whole blood was collected in heparin and the serum was removed by centrifugation. The red cells were washed with normal saline, weighed and dissolved in 10 per cent trichloracetic acid. It was found that between 0·3 and 0·5 gm. of red cells dissolved in 8 ml. of trichloracetic acid gave the best results.

A 'Dowex-1' (10 × 100–200 mesh) column, which had previously been washed first with 20 per cent formic acid until free of chloride and afterwards with distilled water, was used for separation. All the trichloracetic acid extract was placed on the column and washed with 10 ml. of distilled water. The glucose-6-phosphate was eluted with 0·2 *M* ammonium formate solution *p*H 7·25. The fructose-6-phosphate was eluted with 0·5 *M* ammonium formate *p*H 7·25. The eluant was collected in separate 25-ml. volumetric flasks and collection was continued until three successive flasks were free of sugar. The colour

Table 1. RESULTS OF DETERMINATIONS DONE ON NORMAL CONTROLS, HETEROZYGOTES AND AFFECTED INDIVIDUALS EXPRESSED AS GM./100 GM. RED CELLS

Statistical analysis for hererozygotes versus controls of glucose-6 phosphate (G-6-P) showed $t = 5{\cdot}33$ and fructose-6-phosphate (F-6-P) showed $t = 9{\cdot}01$.

	Normals		Heterozygotes		Affected	
	G-6-P	F-6-P	G-6-P	F-6-P	G-6-P	F-6-P
No.	10	10	8	8	4	4
Mean	0·18	0·38	1·10	1·56	1·09	1·30
S.D.	±0·12	±0·14	±0·45	±0·32	±0·34	±0·20
Range	0·05–0·37	0·12–0·57	0·70–2·17	0·86–2·07	0·80–1·67	1·15–1·62

was developed with anthrone reagent and read at 620 mμ in the Beckman *DU* spectrophotometer.

The results were compared with those obtained from standard solutions of glucose-6-phosphate and fructose-6-phosphate and expressed as gm./100 gm. of red cells.

The results from 10 normal controls, 8 heterozygotes (parents of affected children) and 4 patients with von Gierke's disease are given in Table 1. It is apparent that the levels of glucose-6-phosphate and fructose-6-phosphate in the red cells of heterozygotes are significantly different from those of the normal controls and more closely resemble that of those with the disease.

These findings are in agreement with the data of Wagner, Meyerriecks, and Sparaco[7], who demonstrated the accumulation of phosphorylated intermediates of the glycolytic cycle in the peripheral blood of patients with von Gierke's disease. While the results in a single individual must be interpreted with caution, the abnormal values for glucose-6-phosphate and fructose-6-phosphate in a group of known heterozygotes suggest that this may be a phenotypic expression of a single recessive gene for von Gierke's disease. This would provide additional confirmation for the view that the lack of glucose-6-phosphatase is the primary lesion in the disease and extend the concept of being able to detect heterozygous carriers biochemically, as has been shown in the abnormal hæmoglobins[8], phenylketonuria[9] and galactosæmia[10].

We wish to express our appreciation to Drs. Howard Traisman and Ira Rosenthal for sending three of the cases and to Drs. Robert Dowben and Richard Wagner for advice regarding the laboratory methods.

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An Enzymatic Basis for the Acceleration of Ciliary Activity by Negative Air Ions

IT has recently been shown that small negative air ions accelerate the tracheal ciliary activity of mammals both *in vitro* and *in vivo*[1,2]. The subsequent discovery that the actual mediator of these effects is negatively ionized oxygen[3] suggested the possibility of a direct action by negative air ions on one or more of the respiratory enzymes. This seemed increasingly likely when it was found that: (*a*) dilute solutions of sodium azide (as low as 1×10^{-5} molar) inhibit ciliary activity; (*b*) the hæmoglobin of animals killed with carbon dioxide recovers its bright red colour more rapidly in a negatively ionized atmosphere than in ordinary air.

Accordingly, a modified Keilin–Hartree pig heart homogenate[4,5] was prepared and the effect of (–) air ions on its catalytic activity was studied.

The rate of conversion of succinate to fumarate by the homogenate was followed by observing the increase in optical density of the mixture at 250 mμ[6]. Test solutions were exposed in a variety of ways with substantially the same results; in the most convenient method, 0·9 ml. 1 molar disodium succinate, 2·0 ml. boiled and cooled 0·2 molar phosphate buffer at *p*H 7·3, and 0·1 ml. heart homogenate (1 : 10 dilution) were combined in a Beckman silica glass cuvette. After the zero-time reading, the cuvettes were placed in specially designed chambers which permitted exposure to air ions while the solutions were being stirred with magnetic stirrers. Unipolar ion densities of 1×10^8/cm.^{2}/sec. at the fluid–air interface were delivered by 'Wesix' ionizers[7,8] consisting of tritium in a sealed foil with a reversible rectifying circuit to permit selection of either (+) or (–) air ions. At regular intervals the cuvettes were removed and their optical densities read in a Beckman *DU* spectrophotometer. Experiments were run at room temperature; periodic readings with an electronic

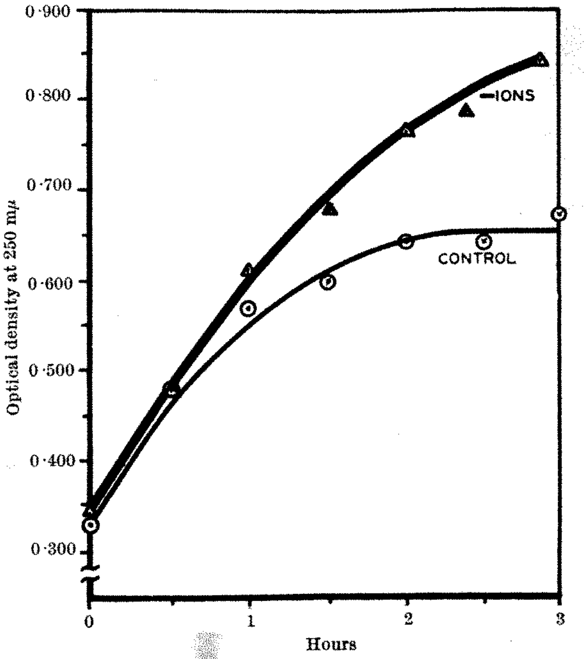

Fig. 1. The rate of conversion of succinate to fumarate by a Keilin–Hartree pig-heart homogenate in normal and negatively ionized atmospheres

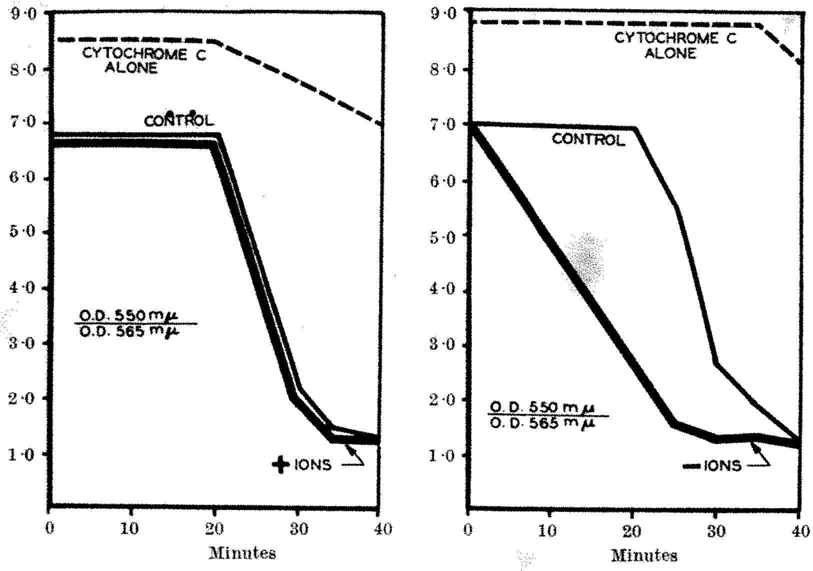

Fig. 2. The re-oxidation by cytochrome oxidase in normal and ionized atmospheres of cytochrome *c* reduced by sodium hydrosulphite. The dotted line shows the behaviour of cytochrome *c* in the absence of cytochrome oxidase in ionized and un-ionized atmospheres

thermometer established that there was no temperature variation between test and control samples.

As shown in Fig. 1, fumarate formation was more rapid in the negatively ionized sample. Positive ions were without effect.

In order to localize further the action of negative ions, experiments were performed on the rate of oxidation of cytochrome *c* alone and on cytochrome *c* plus heart homogenate. A 50-micromolar solution of commercial horse-heart cytochrome *c* ('Sigma') in 0·2 molar phosphate buffer at *p*H 7·3 was reduced with sodium hydrosulphite; 3 ml. samples were placed in control and ionizing chambers; re-oxidation was followed by regular spectrophotometric readings at 550 mμ and 565 mμ according to Paul's method[9]. Positive and negative air ions were without effect on the re-oxidation of cytochrome *c* alone. However, when 0·1 ml. of the cytochrome oxidase-containing Keilin–Hartree homogenate (1 : 10 dilution) was added to the solution, negative ions had a distinctly accelerating effect on the re-oxidation of cytochrome *c*; positive ions had no effect (Fig. 2).

Since sodium hydrosulphite may react with air to form hydrogen peroxide, experiments were performed in which the cytochrome *c* was reduced by either cysteine or ascorbic acid. The results were similar (Table 1). Preliminary exposure of the reductant alone (in solution) to (+) or (−) ions in no way altered the efficacy of the reductant.

It thus appears that negative air ions act directly on cytochrome oxidase, or else form a radical upon contact with water which acts directly on cytochrome oxidase. These experiments provide a reasonable explanation for the accelerating action of negative air ions on the tracheal ciliary rate. They fail to explain, however, the markedly inhibiting effects of positive air ions on the ciliary rate[1,2].

Table 1. RE-OXIDATION BY CYTOCHROME OXIDASE IN NORMAL AND NEGATIVELY IONIZED ATMOSPHERES OF CYTOCHROME *c* REDUCED BY OTHER METHODS

Time of exposure (min.)	Ratio $\frac{\text{Optical density at 550 m}\mu}{\text{Optical density at 565 m}\mu}$ (Cysteine-reduced) (C)	(−)	(Ascorbic acid-reduced) (C)	(−)
0	7·7	7·7	4·5	4·8
40	6·9	6·5	3·5	3·5
60	5·5	1·5	3·0	2·6
80	1·3	1·3	2·5	2·1

Taken in conjunction with the observed action of negative air ions on hæmoglobin, these experiments support the postulate that: it is the distinctive ability of negative air ions—or, more precisely, negatively ionized-oxygen—to react more rapidly with certain iron porphyrin compounds that is responsible for many of their physiological effects (that is, the decrease in respiratory-rate, the increase in the rate of tracheal ciliary beating, the increase in the rate of mucus flow).

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The opinions advanced on this report must not be construed as representing the official views of the U.S. Naval Service.

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Changes in Serum Transaminase Activity following Myocardial Damage due to Lymphatic Congestion

LIGATION of the paracardial lymphatic glands and of the main paracardial lymphatic trunks results in myocardial damage and pathological changes of the electrocardiogram[1]. It is now well known that myocardial damage due to coronary occlusion is accompanied by increase of serum transaminase activity[2,3]. Starting from these facts we investigated the changes in serum transaminase activity following lymphatic obstruction.

The experiments were carried out in dogs of both sexes with average weights of 10–12 kgm. In 7 dogs under chloralose anæsthesia (0·1 gm./kgm. bodyweight) and sterile conditions a thoracotomy was performed on the right side; the paracardial lymphatic glands, the right lymphatic trunk and the

Table 1

	Glutamic-oxaloacetic acid transaminase				Glutamic-pyruvic acid transaminase			
	Operation		Sham operation		Operation		Sham operation	
	Before	After	Before	After	Before	After	Before	After
1	95	293	90	106	76	73	54	106
2	71	210	55	108	48	106	40	35
3	149	310	117	146	81	118	48	95
4	144	196	93	165	36	158	96	82
5	103	296	143	108	48	75	81	93
6	95	305	—	—	67	223	—	—
7	139	324	—	—	—	—		
No. of animals	7	7	5	5	6	6	5	5
Mean	114	276	100	127	59	126	64	82
Mean changes	163		27		66		18	
Difference of changes	$\bar{x}$	136			48			
	s	49·39			49·45			
	t	4·709			1·602			
	P (%)	$<0·1$			>10			

thoracic duct were ligated[4,5]. Sham-operations consisted of thoracotomy in three animals, and thoracotomy plus ligation of cervical glands and the thoracic duct in two animals. Transaminase activity was determined by Umbreit's method in blood drawn daily before and after intervention[6].

Results are given in Table 1. Maximal values up to 3 days before and after intervention are shown. It is evident that glutamic-oxaloacetic acid transaminase activity in sera after intervention increased significantly compared with the controls. Changes in serum glutamic-pyruvic acid transaminase activity were not significant.

Lymphatic obstruction as described above results in the majority of cases in a varying degree of histological change in the myocardium. This is proved by the increased activity of serum glutamic-oxaloacetic acid transaminase. This rise in glutamic-oxaloacetic acid transaminase activity after myocardial damage is analogous to the rise in glutamic-pyruvic acid transaminase activity after hepatic damage[7,8]. It remains unexplained that lymphatic congestion of the liver due to ligation of the thoracic duct does not bring about changes in serum glutamic-pyruvic acid transaminase activity.

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Effects of X- and Ultra-violet Irradiation on the Incorporation of Phosphorus-32 into Isolated Nuclei of Rabbit Appendix

IN previous studies[1] it was observed that the removal of deoxyribonucleic acid from rabbit appendix nuclei isolated in sucrose severely impairs the incorporation of phosphorus-32 into deoxyribonucleic acid, ribonucleic acid, and into organic acid-soluble phosphate. The lost capacity for incorporation can be restored by the addition of some polyanionic compounds, such as calf thymus deoxyribonucleate, yeast ribonucleate, or chondroitin sulphate. By treating the nuclei with pancreatic deoxyribonuclease in the presence of chondroitin sulphate, we have now succeeded in removing the bulk of deoxyribonucleic acid from the nucleus without appreciably affecting its capacity for incorporation (Table 1). An essentially similar but far more extensive observation has recently been reported by Allfrey and Mirsky[2] on the incorporation of labelled precursors into proteins and ribonucleic acids of calf thymus nuclei. However, the incorporation of phosphorus-32 into deoxyribonucleic acid was rather exceptional in this respect, because it could not be retained by chondroitin sulphate when the removal of deoxyribonucleic acid was too extensive (Table 1). This observation confirms the previous finding using sodium nucleates as the restoring agent[1].

Table 1. EFFECT OF TREATMENT WITH PANCREATIC DEOXYRIBONUCLEASE IN THE PRESENCE OF CHONDROITIN SULPHATE ON THE CAPACITY OF PHOSPHORUS-32 UPTAKE OF ISOLATED NUCLEI

Percentage of deoxyribonucleic acid removed	Total radioactivity (percentage of non-digested control)		
	Deoxyribonucleic acid	Ribonucleic acid	Organic acid-soluble phosphate
68	147	98	111
99	0	98	92

Cf. ref. 1 for the preparation of nuclei, method of incubation, and analytical procedure. The nuclei were first treated with 500 μgm./ml. of deoxyribonuclease (Worthington) in the presence of 5 mgm./ml. of chondroitin sulphate. Undigested controls were incubated in the same medium without the enzyme and chondroitin sulphate. They were then appropriately washed (ref. 1) and incubated with phosphorus-32.

We can thus have nuclei depleted of their deoxyribonucleic acid but still metabolically active. They are obviously interesting material for examining the role of deoxyribonucleic acid in the development of the irradiation lesion in the nucleus.

Isolated nuclei of rabbit appendix are much more resistant to X-irradiation *in vitro* than the lymphatic cells isolated from the same organ. Thus the X-irradiation (cf. ref. 3 for details) up to 580 r. did not affect the incorporation into deoxyribonucleic acid and organic acid-soluble phosphate; that into ribonucleic acid was not affected in some active preparations, but was inhibited by about 50 per cent in other preparations which showed relatively low incorporation into deoxyribonucleic acid (Table 2*B*). The lymphatic cells always showed a definite decrease in the uptake of phosphorus-32 into both types of nucleic acids by an X-ray dose of this order, administered *in vitro*[3].

Irradiation with ultra-violet (8–10 min. at 1 m. from a Toshiba 15-W. germicidal lamp; 16–20 times the dose killing more than 99·5 per cent of *Escherichia coli B*) reduced the incorporation into both ribo- and deoxyribo-nucleic acid by 50 per cent or more. At the lower doses (0·5–2 min.) the incorporation into ribonucleic acid was inhibited to a lesser extent while

Table 2. EFFECTS OF DEPLETION OF DEOXYRIBONUCLEIC ACID IN ISOLATED NUCLEI ON THE DEVELOPMENT OF IRRADIATION-INDUCED INHIBITION OF PHOSPHORUS-32 INCORPORATION INTO NUCLEIC ACIDS

Radiation		Concentration of deoxyribonuclease (μgm./ml.)	Percentage of deoxyribonucleic acid removed	Total radioactivity (percentage of unirradiated control)		
Type	Dose			Deoxyribonucleic acid	Ribonucleic acid	Organic acid-soluble phosphate
(*A*) Ultra-violet	10 min.	0	0	46	38	105
	8 min.	0	0	44	54	93
	10 min.	250	46	20	25	84
	10 min.	500	68	22	14	103
(*B*) X-rays	580 r.	0	0	87	41	91
		250	25	99	88	87
	540 r.	0	0	89	48	83
		500	99	—	110	67

(*A*) The nuclei were first depleted of deoxyribonucleic acid as in Table 1, irradiated, and then incubated with phosphorus-32. Because of the agglutination of nuclei, undigested controls could not be irradiated in these experiments, and are not represented here; instead, the cited values of undigested nuclei are taken from separate experiments. (*B*) The control and irradiated nuclei were incubated with or without nuclease, washed and then exposed to phosphorus-32 as in Table 1.

that into deoxyribonucleic acid was rather enhanced. Again there was no significant effect on the incorporation into organic acid-soluble phosphate (Table 2*A*). It is remarkable that in the present system the incorporation into ribonucleic acid tended to be much more sensitive to X- and ultra-violet irradiation than that into deoxyribonucleic acid, which was not inhibited at all on many occasions.

The removal of deoxyribonucleic acid (up to 68 per cent) completely failed to reduce the inhibitory effect of subsequent ultra-violet irradiation on the incorporation into the two nucleic acids (Table 2*A*). This suggests that the observed effect of ultra-violet irradiation was mediated at least in part by some entity (or entities) other than deoxyribonucleic acid. The removal of deoxyribonucleic acid (25–99 per cent) effaced the effect of X-irradiation which preceded the digestion of nuclei with deoxyribonuclease (Table 2*B*), suggesting that deoxyribonucleic acid was involved in the development of X-ray-induced inhibition of phosphorus-32 uptake into ribonucleic acid of isolated nuclei.

Unfortunately, the completion of this work had to be postponed, because the appendix nuclei become inactive during the cold seasons[1]. Details will be published later together with the results of some supplementary experiments yet to be performed.

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Inhibition of Polynucleotide Phosphorylase by Degraded Ribonucleic Acid : its Reversal by Various Agents

STUDIES in this Laboratory have shown that non-dialysable commercial yeast ribonucleic acid and alkaline degraded polyadenylic acid strongly inhibit the polymerization of polyadenylic acid by polynucleotide phosphorylase from *M. lysodeikticus*[1]. Substantial inhibition also occurs with ribonucleic acid from *B. subtilis* partially digested with ribonuclease. The reaction of the inhibitor with the enzyme preparation is slow and may require up to 30 min. for completion. If the substrate, adenosine diphosphate, is added simultaneously with the ribonucleic acid the rate and extent of inhibition is reduced considerably. Concentrations of yeast ribonucleic acid as low as 10^{-7} *M* (phosphate) can give up to 100 per cent inhibition of synthesis of polyadenylic acid. However, in the presence of these inhibitors the rate of polymerization is autocatalytic and shows a significant lag, the extent of which depends upon the inhibitor concentration. Both the inhibition and the autocatalytic character of the rate-curve can be reduced or abolished by the addition of acridine orange, a *B. subtilis* ribonucleic acid preparation, or polyadenylic acid (Fig. 1).

Extensive digestion of ribonucleic acid from *B. subtilis* or yeast by ribonuclease results in a considerable or complete loss of inhibitory power. Dialysable fractions have been obtained which at concentrations of the order of 10^{-7} *M* reverse the inhibition by yeast ribonucleic acid completely. This material is adsorbed quantitatively by 'Amberlite *IRC*–400(*C*1)' resin and is eluted with 0·002 *N* hydrochloric acid. Control studies with orthophosphate, pyrophosphate and the 2′- and 3′-isomers of guanylic, adenylic, cytidylic and uridylic acids show

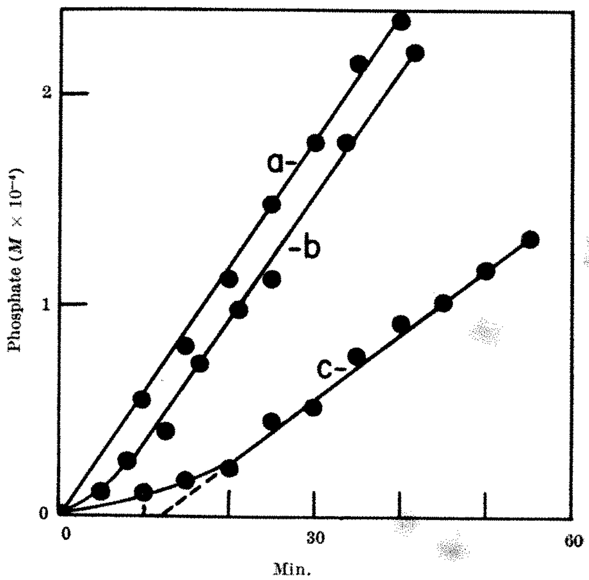

Fig. 1. Effect of yeast and *B. subtilis* ribonucleic acids on the polymerization of polynucleotide phosphorylase. Reaction mixture consisted of polynucleotide phosphorylase 113 from *M. lysodeikticus*, 0·017 *M tris*(hydroxymethylamino)methane buffer (*p*H 9·0), $1{\cdot}7 \times 10^{-4}$ *M* magnesium chloride, 0·2 *M* potassium chloride, 7×10^{-4} *M* adenosine diphosphate. Mixture was incubated at 37° for 30 min. with inhibitors and/or activators before the addition of adenosine diphosphate. Curve *a*, control; curve *b*, $1{\cdot}8 \times 10^{-7}$ *M* yeast ribonucleic acid, $1{\cdot}8 \times 10^{-4}$ *M B. subtilis* ribonucleic acid; curve *c*, $1{\cdot}8 \times 10^{-7}$ *M* yeast ribonucleic acid. Rate recorded as moles of inorganic phosphate liberated per litre of reaction mixture

no activation effect. The possibility that 2′,3′-cyclic phosphate nucleotides (cyclic-cytidylic and cyclic-uridylic acids) are involved is being investigated. Paper chromatographic studies indicate that the activity is associated with material which behaves like these compounds. Non-dialysable fractions have also been obtained which reverse inhibition by ribonucleic acid; these are probably low molecular weight or 'core' material.

The inhibition is both competitive and non-competitive with respect to adenosine diphosphate, showing a decrease in $V_{\text{max.}}$ and an increase in K_m. The inhibition is maximum at low magnesium concentrations ($< 2 \times 10^{-4}\ M$) and decreases to a constant per cent at optimum and inhibitory concentrations of magnesium ($> 4 \times 10^{-4}\ M$). Inhibition of ribonucleic acid increases from a negligible amount with no salt to a maximum at high salt concentration[1]. The extent of inhibition by contaminating ribonucleic acid depends upon the total acid and the ratio of inhibitory and non-inhibitory acid. Preparations of polynucleotide phosphorylase from *B. subtilis* containing high concentrations of ribonucleic acid (280/260 mμ ratio 0·5) lose activity upon standing; this activity can be recovered almost quantitatively by fractionation with ammonium sulphate or by the addition of acridine orange. Treatment of *B. subtilis* polynucleotide phosphorylase preparations with ribonuclease results in a total loss of enzyme activity, whereas similar treatment of *M. lysodeikticus* preparations shows a negligible effect. *B. subtilis* polynucleotide phosphorylase preparations partially inhibited by contaminating ribonucleic acid fail to show any salt activation, whereas freshly prepared and refractionated material is activated by potassium chloride to the same degree as are preparations from *M. lysodeikticus*[2]. Similar salt activation has been observed with preparations from *B. megaterium*.

All enzyme preparations show some activation by acridine orange. The concentration of dye required for and the extent of activation are an order of magnitude greater with preparations of polynucleotide phosphorylase from *B. subtilis* ($2{\cdot}3 \times 10^{-4}\ M$, 75 per cent, 280/260 mμ ratio 0·5) than with those from *M. lysodeikticus* ($10^{-5}\ M$, 7 per cent, 280/260 mμ ratio 1·4–1·7). The quantity of dye required for maximum activation increases with the concentration of ribonucleic acid in the preparation and also, perhaps, with the ratio of inhibitory to non-inhibitory ribonucleic acid. Excess dye inhibits the reaction[3,4].

The extent of inhibition also depends upon the substrate. In an experiment with $10^{-6}\ M$ yeast ribonucleic acid and *M. lysodeikticus* polynucleotide phosphorylase polymerization of polyadenylic acid was inhibited more than 95 per cent, whereas that of polyuridylic acid was only slightly affected.

The kinetics shown in Fig. 1 resemble those described by Mii and Ochoa[5] with preparations of *A. vinlandii* containing an estimated 3 per cent ribonucleic acid. The autocatalytic rate curve and 'priming' action of polynucleotides cannot be demonstrated with *M. lysodeikticus* preparations unless degraded ribonucleic acid or polyadenylic acid is added. It is of interest to note, also, that salt activation observed with *M. lysodeikticus* polynucleotide phosphorylase has not been reported for *A. vinlandii* preparations, whereas the addition of degraded ribonucleic acid to *M. lysodeikticus* preparations abolishes the salt activation process. Finally, the progressive inhibition on standing of polynucleotide phosphorylase from *B. subtilis*, which can be accelerated by the addition of ribonuclease, produces an enzyme-inhibitor system which resembles the *M. lysodeikticus*–yeast–ribonucleic acid mixture and the *A. vinlandii* preparations. We suggest that the results obtained with polynucleotide phosphorylase from *A. vinlandii* by Mii and Ochoa[5] and polynucleotide phosphorylase from *M. lysodeikticus* and *B. subtilis* can be explained by a common mechanism, namely, the inhibition of the polymerization process by degraded ribonucleic acid added or present in the enzyme preparations as contaminant and the reversal of this inhibition by the addition of non-inhibitory or 'active' polynucleotides or 'primers'. A similar explanation can account for the specificity toward different substrates by various preparations of polynucleotide phosphorylase from *M. lysodeikticus* reported by Olmsted[6]. It appears probable that the specificity of priming[5] by different polynucleotides[7] is related to the specificity of inhibition.

The mechanism of inhibition probably involves the 3′-phosphate-ended groups of the polynucleotides[1]. Judging from the initial studies with degraded ribonucleic acid, a minimum molecular weight is necessary for the inhibition. The reversal of inhibition by acridine orange is presumably the result of the specific reaction of the 3′-phosphate-ended groups with the dye to form complex II[3,8]. Reversal of inhibition by highly polymerized *B. subtilis* ribonucleic acid or polyadenylic acid suggests a competitive displacement of the 3′-phosphate-ended polymers from the active enzyme site. The partial reversal of inhibition with increasing substrate concentrations is in conformity with the earlier finding[8] that increased adenosine diphosphate concentrations increase the concentration of molecules of polyadenylic acid. The fact that there is a non-linear relationship between substrate and polymer concentrations may explain the non-competitive character of the inhibition. The autocatalytic nature of the inhibited catalysis of synthesis of polyadenylic acid reflects the increase in concentration of polymer molecules during the reaction[8], that is, the *de novo* synthesis of polymer.

The mechanism of action of the dialysable and non-dialysable fragments of ribonucleic acid is more obscure but may be related to the findings reported by Heppel[9] that 3′-phosphate-ended oligonucleotides activate *A. vinlandii* polynucleotide phosphorylase. The fact that they are not incorporated into the products suggests that they may be acting as templates. However, it appears highly probable that the activation by the dialysable material may be via the formation of oligonucleotides from the cyclic-nucleotides as described by Heppel, Whitfeld and Markham[10].

Irrespective of the underlying mechanisms associated with these results, the significant conclusion to be reached is that polynucleotides, through their activation and inhibitory effects, can alter the specificity of the polynucleotide phosphorylase enzyme toward different substrates. This is believed to be brought about not by the addition of monomers to preformed 'primer'[5,8] but by the alteration of the *de novo* synthesis of polynucleotides. It is interesting to speculate whether such a mechanism is at work in the cell in the duplication of ribonucleic acid.

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Neuronal Dye-Sorption as a Histochemical Indicator of Nervous Activity

PROTEIN extracts from electrically stimulated nervous tissue have been reported to undergo changes resembling those of reversible denaturation[1]. Denaturation of protein, however, enhances dye-protein interaction[2]. It was postulated, therefore, that excitation of nervous tissue could be demonstrated histochemically[3].

Since protein in the denatured state has more ionized tyrosine hydroxyl and cysteine sulphydryl groups available than in the native state, iodination, by lowering the *pK* of the protein, will further increase its affinity for basic dyes[4]. Based on these considerations, the following technique has been developed.

Preservation of the living central nervous system tissue was achieved by immediate submersion into liquid nitrogen. Sections 3μ in thickness were cut in the cryostat at −10° C. and mounted on slides by warming with the fingertip. The sections were then treated in 0·5 per cent w/v of iodine in 95 per cent ethanol for 1 min. at room temperature. Descending concentrations of alcohol and finally distilled water were used to remove non-reacted iodine. The sections were then stained in a *tris*-buffered aqueous 1 per cent methylene blue hydrochloride (*C.I.* No. 922 ; Nat. Aniline dye) solution of *p*H 6·9[5]. Treatment with two changes of aqueous 15 per cent sodium chloride solution prior to rinsing in distilled water and mounting in lævulose or preferably in Lillie's cellulose caprate retarded leaching of the dye. Each step has been standardized.

This staining procedure has been applied to the brain tissue of male Sprague–Dawley rats 90–100 days old. Excitation was produced by either electroconvulsive shocks or by intraperitoneal administration of 0·45 mgm. of picrotoxin/100 gm. body-weight. Animals anæsthetized by 6 mgm./100 gm. body-weight of intraperitoneal nembutal served as controls. At the peak of excitation or depression the animals were instantaneously decapitated in such a way that the head dropped into liquid nitrogen. One minute later the heads were cut in frontal sections by a band saw and the brain tissue removed and blocked for sectioning. During this procedure the tissue remained frozen.

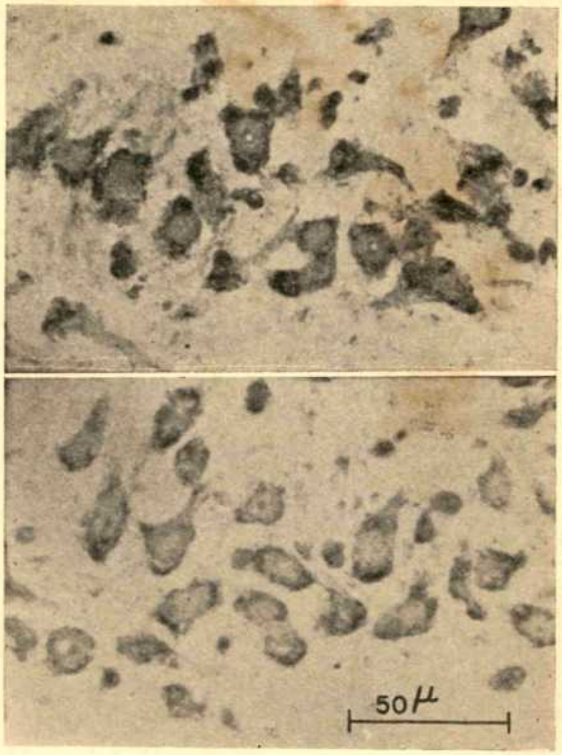

Fig. 1. Rat brain. Large pyramidal cells of hippocampus stained with methylene blue. Above : after excitation with picrotoxin ; below : after depression with nembutal

Excited and control brains were sectioned immediately and mounted on the same slide for comparison. Care was taken to obtain microscopic preparations of corresponding topographical areas.

Surfaces of neurons of excited central nervous system tissue were consistently stained more intensely than surfaces of non-excited, depressed nerve cells. This difference in intensity can only be observed under the microscope (Fig. 1). In addition to the surface of the excited ganglion cell body, the dendrites were also found to be stained to a degree not matched by the control preparations. The nuclei of the nerve cells were not demonstrable. Although glial nuclei are distinctly stained, no consistent differences in staining intensity could be observed between excited and depressed tissue.

Similar findings were revealed in brain sections of twenty-two day old *DBA*–2 mice. In this case excitation was produced by seizures following sonic vibrations of 90 decibels of 1-min. duration. Those litter mates which did not show convulsions under identical conditions served as controls.

Preliminary studies indicate that another phenothiazine derivative, chlorpromazine hydrochloride, follows the same pattern of differential sorption as does methylene blue. When chlorpromazine is used as a 'colourless dye' the differences in sorption must be viewed under a fluorescence microscope.

The nature of the morphological and/or chemical structures involved in the differential sorption of certain phenothiazines has yet to be determined. Pertinent investigations are under way. It is also planned to measure the uptake of dye quantitatively. In connexion with the results reported here it is intriguing to recall that Bodoni[6] observed the tranquillizing action of methylene blue on agitated mental patients as early as 1899.

This work was carried out with the technical assistance of Thomas P. Biggert. The active interest and helpful suggestions of Dr. B. Pasamanick are gratefully acknowledged. Dr. S. Levine kindly placed the *DBA*–2 mice at our disposal. Smith, French and Kline courteously supplied the chlorpromazine hydrochloride.

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PLANT PHYSIOLOGY

Gibberellic Acid and Growth Correlations

AMONG other effects, gibberellic acid may alter plant-growth correlations by decreasing the inhibitory action of leaves and storage organs. Previous work[1–3] has shown that species of *Bryophyllum*, *B. crenatum*, *B. verticillatum* and *B. daigremontanum* do not flower if kept continually under either long- or short-day conditions. To induce flowering, long-day plants showing long internodes and petiolated oval leaves must be exposed daily for 10 days to 12-hr. illumination or less, whereas short-day plants with their very short internodes and round, almost sessile, leaves must be exposed for 20 days to a long day of 13 hr. or more and then to short-day conditions for a further 10 days. These plants were therefore described as long-short-day plants[4]. The long-day plants could not be induced to flower by treatment with gibberellic acid. Bünsow and Harder were able to induce elongation and flowering of long-day plants grown under short-day conditions by treatment with gibberellins obtained from the fungus[5] and from unripe bean seeds[6]. The same result was obtained in our laboratory by treatment with gibberellic acid of material of *Bryophyllum crenatum* which had been maintained in the form of rosettes for 12 years by continuous exposure only to short-day conditions. If, however, after treatment with gibberellic acid these short-day plants were exposed to continuous illumination or to long-day conditions, they failed to form flower primordia although they elongated strongly, forming long internodes and new oval petiolated leaves. Thus gibberellic acid can replace the long-day requirement but not the quite specific flower-inducing effect of the short day. Extremely rarely a single flower appeared in the axil of one of the upper leaves of the rosette plants grown under short-day conditions; this was only observed in the spring of 1949 in two out of many hundred plants grown in a 9-hr. day.

Studies have also been made with the long-day plant *Circaea intermedia*, which was the first in which the inhibiting effect of higher concentrations of indole-3-acetic acid on flowering was demonstrated[7]. Weak plants which had remained apparently vegetative even under long-day conditions elongated considerably and flowered when a paste containing 0·5 per cent of gibberellic acid was applied to the stem apex. The same effect is produced by defoliation of the upper part of the stem and so removing the leaves controlling growth inhibitions. Tubers of this plant gathered in autumn and then treated at the apex with gibberellic acid paste formed many long orthotropic filamentous shoots whereas control tubers smeared with pure lanolin either remained dormant or developed slowly growing horizontal stolons with tubers at the end. A similar change in geotropic response also occurred with axillary shoots. When axillary buds in one-node cuttings taken from the basal part of the stem were treated with gibberellic acid paste they developed into long and very thin vertical shoots, whereas the control buds smeared with pure lanolin grew into plagiotropic stolons which tuberized. Thus the correlative growth inhibitions of leaves and tubers, so important for the correlations of growth processes, may be decreased by application of gibberellic acid, which thus replaces the growth-promoting effect of the roots.

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Chlorophyll a in some Corals and Marine Plants

ASSOCIATIONS of algae and marine invertebrates are common in coral reefs of tropical seas. According to Yonge[1,2] the algal components of corals obtain carbon dioxide and nutrients from the associated animals; but just what advantages of pseudo-symbiosis accrue for the individual animal body has not been clearly demonstrated. Odum and Odum[3] have expressed the view that the algal-coelenterate complex of tropical coral reefs is "a highly integrated ecological unit (comparable to the algal-fungal complex of a lichen) which permits cyclic use and re-use of food and nutrients necessary for vigorous coral growth in tropical 'desert' waters having a very low plankton content". New approaches to this problem of symbiosis have been developed recently by the growing of single-celled zooxanthellæ isolated in pure cultures from marine jelly fish and sea anemones, and demonstration that these are in reality motile dinoflagellates[4]. It has not been clearly shown whether these photosynthetic flagellates contribute food supplies to the animal polyps.

If the trophic structure of a coral reef is a pyramid of biomass with a considerable excess of producing organisms at the base, then it becomes important to know more about the synthetic potential of the different kinds of primary producers in the reef. Quantitative analysis of pigments can give a measure of the assimilatory potential of green organisms which absorb radiant energy used in photosynthesis. Although various methods, such as the oxygen method and carbon-14 technique, may give precise indications of actual productivity, it is believed that determinations of the chlorophyll *a* content of plankton, algae, corals, etc., may have considerable significance in various problems concerned with productivity and food relations among groups of organisms in the sea.

The present study attempts to assess the chlorophyll potential of a number of different kinds of corals and sea anemones, and to compare them with other photosynthetic systems of algae and flowering plants in a tropical marine environment. Samples of plants and animals were collected near the Marine Laboratory at La Parguera, Puerto Rico, during March 1958. The pigmented portions of these organisms were ground and extracted with 90 per cent acetone in a mortar. After filtration in subdued light, the extracts were made to standard volume, and their absorption was determined at appropriate wave-lengths in a Beckman spectrophotometer. Calculations of chlorophyll *a* per gram of fresh samples were made according to the method of Richards with Thompson[5].

The general results of this survey can be illustrated by results obtained for representative types of organisms, a few of which are shown in Table 1. A summary of the results, arranged according to ten different groups of chlorophyll concentration, is presented in Table 2. Although the distribution of chlorophyll *a* in plants and animals shows overlap in the lowest four groups of Table 2, it is obvious that the concentration of pigment is relatively low in most of the animals studied. Among the various corals and anemones, high chlorophyll values were found in gorgonian corals and in *Condylactis*. Seven species of plants showed chlorophyll *a* contents greater than the maximum observed in any of the animals.

Table 1. CHLOROPHYLL *a* CONTENT (µGM./GM. WET WEIGHT) AND PIGMENT DENSITY RATIOS IN REPRESENTATIVE MARINE ORGANISMS OF PUERTO RICO

Organisms	Chlorophyll *a*	D_{480}/D_{665}
Corals		
Briareum asbestinum	97	6·1
Diploria clivosa	25	4·2
Gorgonia flabellum	218	6·0
Plexauropsis crassa	164	5·6
Porites furcata	30	5·4
Anemones, etc.		
Condylactis gigantea	336	4·2
Stoichactis helianthus	115	4·2
Zooanthus sp. (green)	138	5·3
Algae		
Caulerpa verticillata	912	1·5
Cladophoropsis membranacea	217	1·9
Dictyota divaricata	109	2·7
Halimeda tridens	631	1·7
Penicillus capitata	500	1·7
Udotea flabellum	806	1·7
Flowering plants		
Cymodocea manatorum	296	1·6
Diplanthera wrightii	468	1·8
Rhizophora mangle	318	1·8
Thalassia testudinum	655	1·6

Table 2. DISTRIBUTION OF CHLOROPHYLL *a* AMONG 23 MARINE PLANTS AND 30 ANIMALS GROWING IN SHALLOW WATERS NEAR LA PARGUERA, PUERTO RICO

	µgm. of chlorophyll *a* per gm. of tissue									
	1–100	101–200	201–300	301–400	401–500	501–600	601–700	701–800	801–900	901–1,000
Plants*	5	4	5	2	3	0	2	0	1	1
Animals	23	5	1	1	0	0	0	0	0	0

*Leaves of *Thalassia* occur in the 601–700 class, but chlorophyll *a* of the whole plant body falls into the low 1–100 class, along with the majority of corals.

Considerable variation occurred in the different samples of the species which were tested. Thus, five determinations for *Thalassia* gave results ranging from 462 to 655 µgm./gm. of fresh leaf tissue. When the value of 655 for *Thalassia* leaves is recalculated for the whole plant, then the result comes to only 73 µgm./gm. of plant body. If the calculation of pigment on the basis of the whole functional body of plants and animals gives a fair comparison, then many corals would be found to contain chlorophyll *a* in concentrations as high as those of common marine algae and flowering plants. The presence of significant amounts of chlorophyll *a*, along with other pigments in the fauna of coral reefs, is related chiefly to the presence of numerous unicellular algae, which live in association with the polyps. In some of the stony corals, green and blue green algae occur also in the hard structure. Studies on the overall productivity of these algae in the reef community, and symbiotic exchanges between zooxanthellæ and polyps are being continued.

The ratio of yellow to green pigments may have some significance in estimating the photosynthetic potential of carbon dioxide – light assimilatory systems. According to the data discussed by Richards with Thompson[5], carotenoid absorption may be best observed at wave-length 480 mμ, while chlorophyll *a* shows an absorption maximum near wave-length 665. Hence, we have chosen a simple expression of pigment density ratio = D_{480}/D_{665}, which roughly relates the optical density of the yellow pigments to that of the green pigments. Pigment density ratios for 16 corals, 5 anemones, 18 algae, and 4 phanerogamic plants have been calculated. Typical results are shown in Table 1. The range and average of pigment density ratios among the various groups are as follows: coral range 4·2–6·1, average 4·9; anemone range 4·2–5·3, average 4·6; algae range 1·5–2·7, average 1·8; phanerogam range 1·6–1·8, average 1·7. The leaves of flowering plants and the thalli of green algae commonly show a ratio of about 1·7, whereas the ratio found in corals and anemones is generally greater than 4·6. Studies on the pigment density ratio of the internal green algal bands and the outer brown polyp regions of two corals, *Porites furcata* and *Diploria clivosa*, gave ratios of about 1·6 for the green internal bands and approximately double this value for the polyp region. It appears that photosynthetic capacity is greatest in organisms having a low pigment density ratio, that is, a high proportion of chlorophylls to carotenoids. Carotenoids seem to be unusually abundant in the symbiotic corals and certain kinds of sea anemones.

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BIOLOGY

Reactivation of Heat-inactivated Poxviruses: a General Phenomenon which includes the Fibroma–Myxoma Virus Transformation of Berry and Dedrick

IN 1936, Berry and Dedrick[1] reported that active myxoma virus could be recovered from rabbits injected with mixtures of heat-inactivated myxoma and active fibroma virus. Because their experiments were suggested by Griffith's[2] studies on the transformation of pneumococcal types, Berry and later investigators called heated myxoma virus the "transforming agent" and the phenomenon "fibroma-myxoma virus transformation". However, Berry recognized that reactivation of the heat-inactivated myxoma rather than transformation of the active fibroma virus was a possible alternative mechanism.

The term 'transformation', as used in bacterial genetics, has been defined as the heritable modification of the properties of one bacterial strain by an extract derived from cells of another strain. The active material responsible for transformation is deoxyribonucleic acid. There is no evidence that the phenomenon described by Berry and Dedrick is an example of transformation, in this sense. The process is better interpreted as reactivation of the inactivated virus, and we shall use that term henceforth.

Berry's results have been repeatedly confirmed, but further analysis of the mechanism was precluded by the irregular results obtained in intact animals. Recently, Kilham[4] showed that the Berry–Dedrick phenomenon could be demonstrated with regularity with heat-inactivated myxoma virus and active fibroma virus, in cultures of rabbit, monkey and squirrel kidney cells. With collaborators[5] he has described the effects on the heated myxoma virus component of some physical and enzymic treatments.

The definition of several independent genetic markers of vaccinia virus suggested that it might be a more suitable agent for the study of the mechanism of the Berry–Dedrick phenomenon than myxoma and fibroma viruses. The strains of vaccinia virus used for most experiments discussed here were those employed previously for recombination experiments[6]. Their biological characters are set out in Table 1.

Table 1. BIOLOGICAL CHARACTERS OF TWO STRAINS OF VACCINIA VIRUS (FROM REF. 6).

Designation of strain	Morphology of pock on chorioallantoic membrane	Production of hæmagglutinin	Heat resistance	Mouse virulence	Rabbit virulence
RP	hæmorrhagic ulcerated (U^+)	nil (A)	high (T^+)	high (VM^+)	high (VR^+)
V-Led-7N	white non-ulcerated (U)	high (A^+)	low (T)	low (VM)	low (VR)

The appropriate symbols for phenotypes are shown in brackets.

The virulent strain, *RP*, was used as the inactivated agent. After heating for 2½ hr. at 55° C. in 0·1 *M* sodium chloride, 0·01 *M* citrate, at *p*H 7, suspensions which originally contained about 10^8 pock-forming units/ml. were shown to be non-infective when inoculated on the chorioallantoic membrane, with passage of the membrane two days later. All heated material used was inactive by this test, which was the most sensitive available. Mixtures of heated *RP* and active *V-Led-7N* were inoculated intracerebrally in mice, and brains were removed for assay on the chorioallantoic membrane at various intervals. Such brain suspensions yielded clones of virus indistinguishable from *RP* in all the characters listed in Table 1, as well as recombinants between *RP* and *V-Led-7N*. Both the recombinants and *RP* were recovered as early as 18 hr. after inoculation. Since *V-Led-7N* multiplies to a limited extent only in the mouse brain, it was found only in the early stages. This result is directly comparable to Berry's observations, for living virulent virus was recovered from an animal inoculated with a mixture of heat-inactivated virulent virus and a related active attenuated strain. It also showed something that could not be determined with myxoma-fibroma, namely, that some clones of virulent virus resembled the original heat-inactivated virus in all the characters that could be examined, and that others, although highly virulent, were recombinants.

The mouse brain was used to test the capacity of heated *RP* to be reactivated after further physical, chemical and enzymic treatments. Suspensions of *RP* could be heated at 55° C. for more than 7 hr. before the capacity for reactivation was greatly reduced, but this was destroyed in a few minutes at 60° C. In contrast to the report of Smith[7] (for which detailed support has never been published) attempts to dissociate protein and deoxyribonucleic acid have so far been unsuccessful. As Kilham and his collaborators[5] found with myxoma virus, various forms of enzymic digestion of the heat-killed virus (trypsin and deoxyribonuclease at *p*H 11, pepsin at *p*H 3·5, papain at *p*H 7·5 and above) leave the capacity for reactivation intact and associated with particles deposited in the same centrifugal field as vaccinia virus.

Reactivation of heated *RP* was also observed after the inoculation of mixtures of heated *RP* and active *V-Led-7N* into cultures of HeLa cells, and on the chorioallantoic membrane. Use of the chorioallantoic membrane had the advantage that it allowed the direct demonstration of reactivation without the necessity of passage. When about 10^8 particles (originally 10^7 pock-forming units) of heated *RP* were inoculated on the chorioallantoic membrane together with 20–30 pock-forming units of active *V-Led-7N*, about half the pocks seen two days later were of the U^+ type, that is, they resembled those of *RP*. Analysis of 32 clones from U^+ and U pocks showed that nine resembled *V-Led-7N*, 11 resembled *RP* and 12 were recombinants. Using the chorioallantoic membrane, reactivation of heated *RP* has been induced not only by another strain of vaccinia (*V-Led-7N*) as the active agent but also by all the other members of the poxvirus group that have been tested, namely, cowpox, ectromelia, myxoma, fibroma and fowlpox. The reverse process, reactivation of heated *V-Led-7N* by active *RP* and by ectromelia virus, has also been accomplished. The phenomenon is probably a general one, demonstrable with many different combinations of pox viruses, although the ease of recognition of the reactivated component differs. Experiments with several other viruses which produce pocks on the chorioallantoic membrane yielded negative results; no reactivation of heated *RP* was observed when the active virus component was herpes simplex virus, influenza virus strain *WSE*, or Murray Valley encephalitis virus.

The search for recombinants between *RP* and reactivating viruses other than *V-Led-7N* is not yet completed, but reactivation of heated *RP* invariably yielded virus indistinguishable from *RP* in all the characters set out in Table 1 (U^{+} A T^{+} V ($M^{+}R^{+}$)). The recovery of such clones from mixtures of viruses as dissimilar as *RP* and fibroma or fowlpox renders unlikely Berry's original idea that the heat-inactivated component 'transforms' the active virus. Reactivation of the heated virus by the active agent is a more plausible explanation. Whether reactivation is accomplished by some sort of genetic interaction, or whether the primary mechanism is repair of some non-genetic damage of the heated virus, with recombination as a possible secondary event, cannot yet be decided.

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Relation of Extracellular to Intracellular Potential Records from Single Cardiac Muscle Fibres

IN the atrial muscle of the heart the rate of depolarization (70–100 V./sec. at 30° C.) is so much more rapid than that of repolarization (less than 1·0 V./sec.) that the two events cannot be confused, and a comparison may be made between records obtained from the inside and outside of a single fibre during the depolarization phase only[1]. Pairs of isolated rabbit atria were mounted horizontally in oxygenated fluid and made to beat at constant frequency in response to electrical stimuli applied to the tip of the left atrium. Contractions were measured with a transducer, and action potentials from the left and right atria were recorded with pairs of small bipolar external electrodes, from which conduction velocity was calculated. Glass microelectrodes, filled with potassium chloride, with tips less than 0·5μ across and resistances of 10–30 MΩ, were introduced under visual control into single fibres on the endocardial surface by a manipulator which could be moved smoothly over distances as small as 2μ.

Fig. 1*A* shows a record of a cardiac action potential obtained with a microelectrode just touching the surface of a fibre. There were four phases : (1) upward positive, (2) fast downward negative, (3) upward positive to just above the base-line, (4) slow return to zero. The electrode was then lowered, and suddenly recorded a resting potential of −74 mV., indicating that it had penetrated a fibre. Fig. 1*B* shows the contraction of the atria (lowest trace), and the intracellular action potential above it. The dotted line represents the zero potential of the electrode when it was extracellular. The vertical trace on the right gives the records from the external bipolar electrodes, and the inset indicates the time to within 0·1 sec.

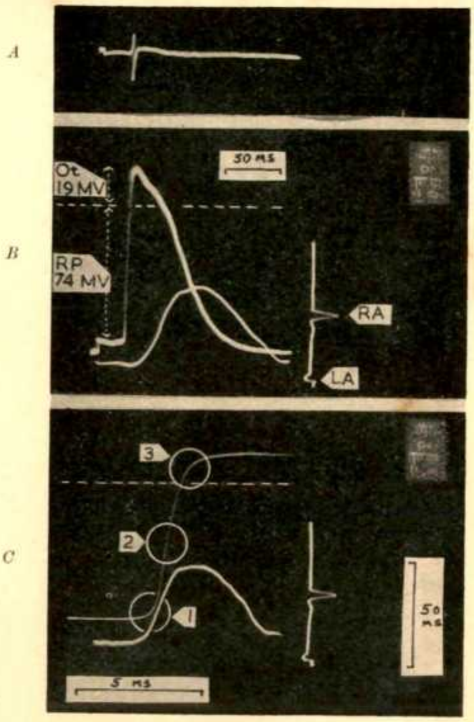

Fig. 1. *A*, Cardiac action potential recorded with microelectrode outside fibre. *B*, Lower trace, contraction ; upper trace, intracellular potential ; *RP*, resting potential ; *Ot*, overshoot ; dotted line, zero potential ; right-hand trace, external records of action potential from left (*LA*) and right atrium (*RA*) ; inset, time of exposure at 11 min., 7·1 sec. *C*, As *B*, except that the sweep recording the intracellular potential was faster. (Photographs not retouched)

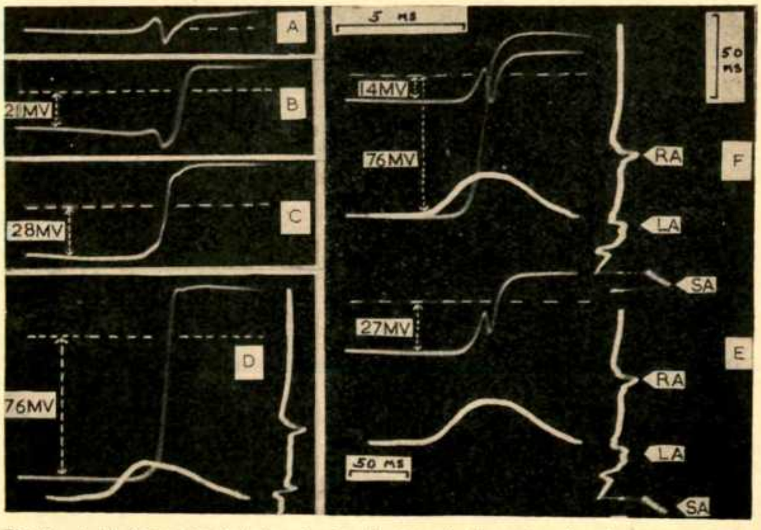

Fig. 2. *A–D*, Four records taken during the introduction of a microelectrode ; *E* and *F*, three records taken during consecutive heart beats to show that the negative phase of the action potential recorded when the electrode was extracellular corresponded to phase (2) of the action potential recorded intracellularly ; *S.A.*, stimulus artefact. (Photographs not retouched)

Comparison of Figs. 1*A* and 1*B* shows that phases (1) to (3) of the extracellular potential were associated with depolarization, and the slow phase (4) with repolarization. In Fig. 1*C* the oscilloscope trace of the intracellular potential had been speeded up

23 times, so that it showed the depolarization only, making the first three phases more distinct. The four phases might be interpreted as follows. (1) Membrane active at a distance and active region approaching the electrode. Both extracellular and intracellular records became positive in phase because the indifferent electrode was in contact with the active (outside negative) region via the extracellular fluid. (2) Active region at electrode. The electrode, when extracellular, was on the negative pole of the 'sodium battery'[2], and on the positive pole when intracellular, so that the two records were out of phase. (3) The intracellular record rose to peak positivity as the inflowing depolarizing current came to an end, and the extracellularly recorded potential also became positive as the active region travelled away from the microelectrode. (4) Resting potential restored as membrane very slowly repolarized. It has been remarked that surface records in a volume of fluid bear some resemblance to the second derivative of the monophasic potential[3], but this does not account for phase 4.

As a rule, when the microelectrode was introduced into a fibre, the full resting potential appeared with great suddenness. Occasionally, the resting potential developed slowly or irregularly, and such records were rejected. Some of these records, however, although valueless as measurements of resting potential, were of interest in showing that a record of resting potential was not a reliable criterion for judging whether an action potential was being recorded from inside or outside a cell. Figs. 2*A*–*D* shows four successive records taken during the penetration of a cardiac fibre. The record of Fig. 2*A* was obtained from an electrode just touching the surface of a fibre, and is comparable with Fig. 1*A*, except that the speed of the sweep recording the intracellular potential was faster. In Fig. 2*B*, a resting potential of 21 mV. had developed, yet the action potential could not be said to be of an intracellular type because phase (2) was negative. In Fig. 2*C*, on the other hand, although the resting potential had increased to only 28 mV., the action potential was of an intracellular type since phase (2) was now positive. In Fig. 2*D* the electrode was fully intracellular, and recorded a stable resting potential of 76 mV., and an action potential comparable with that of Fig. 1*C*.

The relation of the phases of the action potential recorded intracellularly and extracellularly is illustrated by Figs. 2*E* and *F*, in which three consecutive heart beats have been photographed, two of them on the same frame. In Fig. 2*E*, during the first beat, although a resting potential of 27 mV. was observed, the action potential was not of an intracellular type since phase (2) of the action potential was negative. Before the next beat the electrode entered the fibre, and the fast positive phase (2) of the upstroke of the action potential corresponds with the negative phase of the superimposed third record, when the electrode had again come out of the fibre. There was no change in conduction velocity between the beats, because the two superimposed records in Fig. 2*F* of externally recorded action potentials from the left and right atria (to the right of the frame) do not differ measurably from the single similar record in the preceding frame (Fig. 2*E*).

Microelectrodes inside single fibres of frog skeletal muscle do not record to a significant extent potentials occurring in surrounding fibres[4,5], and a tracing such as that of Fig. 1*C* provides no evidence that this is not also true of cardiac fibres. The simplest explanation for the records of Fig. 2, therefore, is that the electrode was at first in a fibre damaged to the extent that the resting potential was abnormally low and the action potential absent (Fig. 2*E*) or attenuated (Fig. 2*C*), but that the electrode was also recording as an external electrode the action potential in a subjacent fibre which it eventually entered (Figs. 2*D* and *F*). In any event it is apparent that the observation of a d.c. potential is inadequate evidence that an action potential superimposed on it is being recorded intracellularly, an assumption which can be made only if (*a*) there is a large and stable resting potential, (*b*) there is no negative component in phase (2) of the action potential.

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Development in a Mutelid Lamellibranch

Although the life-history of lamellibranchs of the family Unionidae has been known for almost a century, little has been recorded concerning members of the related Mutelidae. This taxonomically ill-defined family has representatives in the fresh-waters of Africa, South America and Australia. A glochidial stage similar to that of the Unionidae is said to occur in the development of some reputed mutelids in Australia. At least one South American species produces a peculiar larva to which the name lasidium has been given but its subsequent development is unknown. Nothing has been recorded regarding the development of the African species.

Recent studies have elucidated the life-history of the African species *Mutela bourguignati* (Ancey) Bourguignat 1885, which is depicted in Fig. 1. The stages illustrated are referred to in the text by the relevant letters. The adult female produces numerous minute larvæ (*a*) which, while still within the egg membrane, are brooded in the inner demibranchs of the ctenidia. These larvæ are in some ways similar to the typical molluscan veliger but differ in certain respects, most of the differences being correlated with

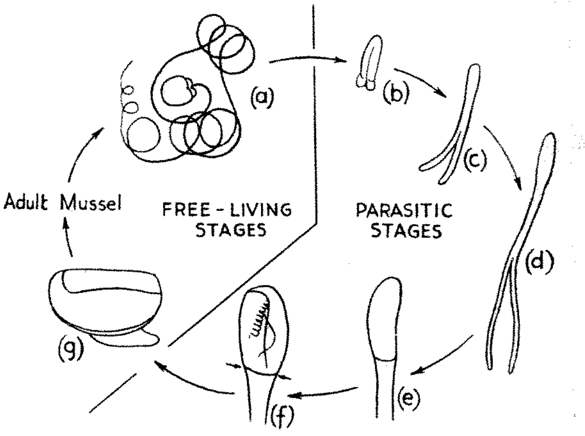
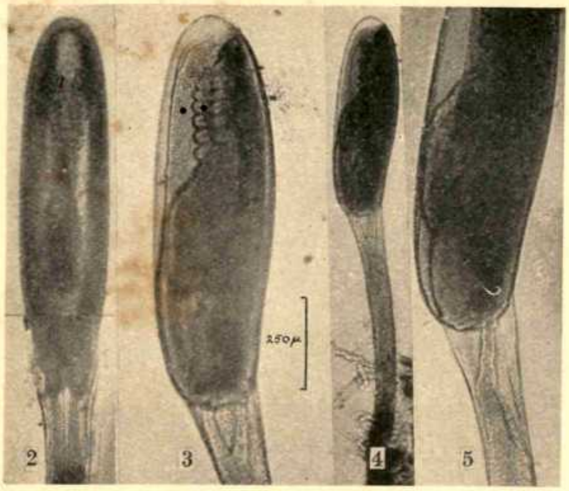


Fig. 1. Life-history of *Mutela bourguignati*. The illustrations are semi-diagrammatic and are not all drawn to the same scale



Figs. 2 and 3. Posterior (distal) extremity of fairly advanced post-larvæ in which, although still completely enclosed within the post-larval cuticle, the rudiments of certain adult organs are well defined. Fig. 4. The same specimen as that shown in Fig. 3 but showing more of the post-larval tube. (The objects adhering to the lower part of the tube are sessile ciliate protozoans which often colonize this region.) Fig. 5. Region where, at a later stage of development, the young mussel and the stalk will part company. In all the photographs, and most clearly in Figs. 2 and 5, the anterior prolongations of the mantle, which extend into the anchoring tubes, can be seen

the subsequent period of parasitism. Most remarkable of these larval features is the possession of an extremely long filamentous tentacle which resembles the tentacle of the glochidium of the Unionidae but is very much longer, being more than 70 times that of the larva itself.

These larvæ are shed through the exhalant siphons of the parent, and such as locate a host attach themselves to the cyprinid fish *Barbus altianalis radcliffi* Boulenger, usually, but not exclusively, to the fins. Attachment is probably effected initially by means of minute hooks with which the larva is provided posteriorly. After establishment on the host a remarkable transformation takes place. The tentacle is lost, and the larval shell, which at this stage consists merely of a thin pellicle and shows no signs of calcification, folds into a minute bivalved structure in which fusion occurs in the mid-ventral line to give, ultimately, a completely enclosed structure. This process is reminiscent of what occurs during metamorphosis of the Scaphopoda, but is carried even further in that both ends of the folded shell are sealed. Two outgrowths arise from the anterior end and penetrate the superficial tissues of the host (*b*). Growth of these structures results in the formation of two completely enclosed tubes (*c*) which serve as organs of attachment and through which nutritive substances are presumably absorbed from the host. With the exception of these structures the post-larva develops outside the host tissues. As a result of the fusion process described, the body of the post-larva is enclosed in a sealed tube the nature of the non-calcareous walls of which is being investigated. This tube grows to a length of about 3 mm. Within its distal extremity the adult mussel is eventually formed. Running from the distal mass of tissue through the proximal part of this tubular structure, and separated from each other by a longitudinal septum of the same material as the outer walls, are two strands of tissue which, as revealed in later stages of development (Figs. 2–5), are morphologically anterior extensions of the mantle. These extend into, and to the extremities of, the anchoring tubes. At this stage the parasitic post-larva is not only unlike a mollusc but also, from its external appearance, could easily be mistaken for a fungal hypha.

Enlargement of the distal extremity and differentiation within it (Fig. 1*d* and *e* and Figs. 2–5) results in the formation of adult organs—mantle, foot, ctenidia, adductor muscles, etc.—and the organic matrix of the adult valves begins to be formed. The periostracum is secreted from the inner face of the outer mantle fold in the manner typical of lamellibranchs. At first this primitive shell material forms a layer inside, and closely adpressed to, the post-larval tube; but subsequent growth and secretion result in a longitudinal split of the tube in that region of the post-larva where the adult structures are forming and along what will be the mid-ventral line of the adult mussel. The post-larval tube material, however, continues to embrace the rudimentary adult valves and to strengthen the ligament region (*f*). Calcareous material is deposited in the valve rudiments and the gut opens to the exterior so that, even before it leaves its host, the mussel can, and does, feed by ciliary action in the typical lamellibranch manner. At this stage, which represents the termination of the parasitic phase of the life-cycle, the organism is clearly recognizable as a typical bivalve attached to the end of a long stalk.

Rupture of the tubular outgrowth at a point near the anterior end of the newly formed valves (indicated by arrows in Fig. 1*f*) results in the release of the young mussel (*g*), which falls to the bottom and commences an independent existence. At the time of its release it has a length of rather less than 1·5 mm. The stalk remains attached to the host.

Not only is such an ontogenetic sequence highly specialized, but also both larval and post-larval stages, and particularly the latter, exhibit features which are unique within the Mollusca. Anatomical studies of the various stages of development are now in progress and a detailed illustrated description of these and a more complete account of the life-cycle will be published in due course.

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Bulbil Formation in *Sedum telephium*

A vegetative plant of a species of *Sedum*, afterwards identified as *S. telephium*, was collected in a hedgerow on Rothamsted Farm on June 9, 1958, and placed with its roots in a jar containing tap water to keep it alive for further study. The jar stood on the laboratory window-sill for three months, when it was observed that, although the specimen failed to flower, bulbils had formed in the axils of the upper leaves—positions in which flowering stems would normally arise. Some axils contained several bulbils as shown in Fig. 1. Each bulbil bore scale-leaves and numerous white roots, each of which had a conspicuous dark root cap. When separated from the parent plant and placed on damp filter paper, each bulbil quickly developed into a new plant. Fig. 2*a* shows such a plant after six days growth and Fig. 2*b* after 13 days growth respectively. At the first two or three nodes the leaves were simple and opposite, but the fourth node produced irregularly dentate leaves typical of the adult plant.

Bulbil formation seems not to have been previously reported in the genus *Sedum*, although Godron[1] men-

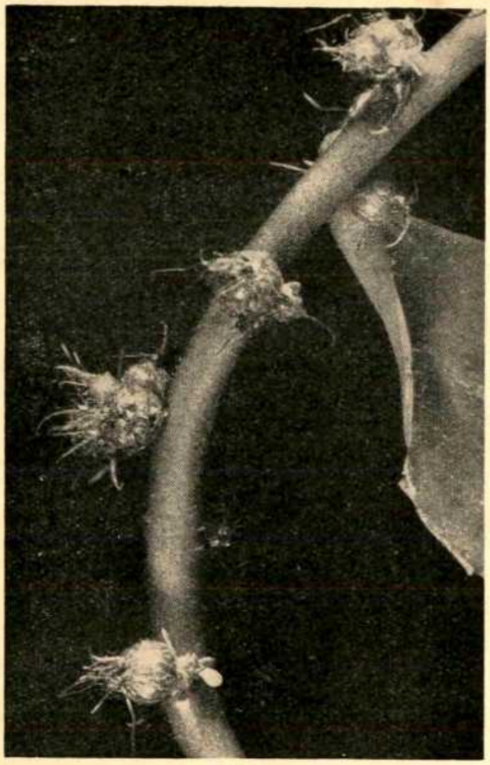
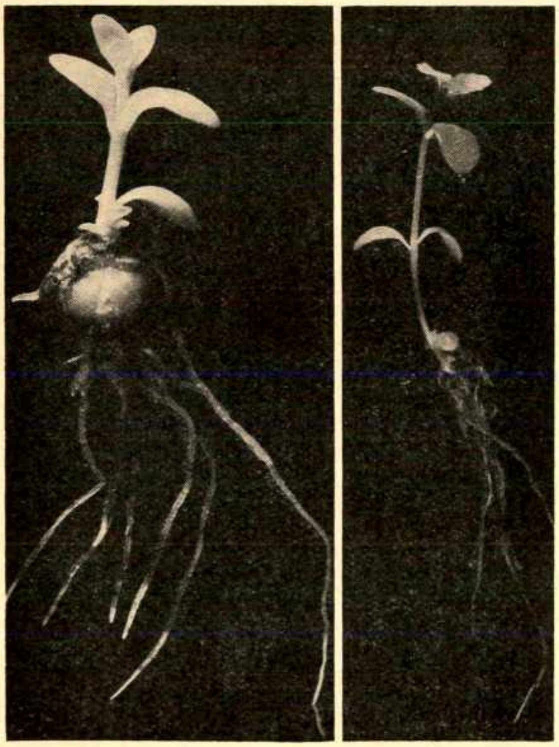


Fig. 1

tions this genus as one containing species with the power to develop buds on the surface of the leaf. Lloyd Praeger[2], in a monograph on the genus *Sedum*, was apparently not aware of the phenomenon of bulbil formation, but points out that some of the *Telephium* section of the genus, notably *S. viviparum* and *S. verticillatum*, produce in the upper part of their annual stems numerous small leafy buds which, when the stems fall, root readily and form new plants. A somewhat similar condition occurs in *Crassula multicarva* and *C. cordata*[3], where small shoots in the inflorescence region bearing two pairs of leaves can function as organs of vegetative propagation. The bulbils described in this communication appear to be an extreme form of such shoots.



(*a*) (*b*)

Fig. 2

Why this specimen formed bulbils is uncertain, but its only supply of minerals was from a small amount of tap water. The possible relationship between bulbil formation and nutrition will be further studied in experiments using solutions of known mineral content.

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Ecology of *Mucor ramannianus* Moller

Mucor ramannianus is one of the commonest fungi occurring in certain acid, sandy soils, and often, in some horizons, may be the only fungus isolated by standard plating methods. In grassland soils at Lakenheath Warren it was confined to those of low *p*H value[1], and Thornton[2] found it to be very common in podsolized soils beneath *Calluna vulgaris* L., but absent from soils of similar derivation beneath mixed oakwood. *M. ramannianus* was a characteristic fungus in six out of nine acid, heath soils examined by Jefferys, Brian, Hemming and Lowe[3], who suggested that its presence was related to the existence of a well-marked iron-pan in the *B* horizon. McLennan and Ducker[4,5] have further suggested that a predominance of *M. ramannianus* is indicative of acid, sandy soil types with a well-defined pan layer. Detailed studies, primarily of a physiological nature, have been described by Müller[6], who concluded that not only the presence of growth factors but also the hydrogen ion concentration of the soil and source of carbon would play an important part in limiting its distribution. *M. ramannianus* was among the commonest species encountered by us in soils and on roots during detailed surveys of the mycofloras of some British dune systems[7] and *Calluna*-heathlands[8]; its distribution was closely related to certain soil conditions which are discussed below. These observations are presented in view of the fragmentary and sometimes conflicting data available on the ecology of this interesting species.

The succession of soil fungi from open sands of the shore to fixed dune in Britain typically culminates in a community resembling that of acid heathland or alkaline grassland. *M. ramannianus* was isolated by the soil plate method[9] from one or more of the acid semi-fixed or fixed zones in all such dune systems investigated, but from none of the alkaline or young acid dunes. The acid dune zones in which *M. ramannianus* attained a frequency of at least 50 per cent were dry dune-heaths dominated by *Ammophila–Carex–Calluna*, *Calluna*, or *Calluna–Pteridium* communities.

M. ramannianus was present in all but two of fourteen distinct inland *Calluna*-heath soils from six counties of England and Wales, but was of very infrequent occurrence in several of these. There was a marked relationship between its frequency of occurrence and the moisture relations of the habitat as indicated by the surface vegetation; indeed, *M. ramannianus* appeared to be less tolerant of wet conditions than *Calluna* itself, and was of infrequent occurrence or absent from soils where plant communities indicating damp soil conditions occurred, that is, *Calluna* in association with *Molinia*, *Erica tetralix* and *Salix repens*.

In both acid dune and inland heath soils the frequency of occurrence increased with depth to a maximum in the humus-poor or leached, subsurface sands. Within the acid dune succession the first distinct subsurface population was found in the dune heath profiles when *M. ramannianus* and *Penicillium restrictum* were characteristically associated together at a soil depths of 6–12 in., often in the absence of other species. Similarly, in dry, inland heaths, *M. ramannianus* was characteristically predominant in specifically poor mycofloras of the A_2 horizons. The lower limit of vertical distribution in dune heaths was often clear-cut although the sand above and below it appeared similar. This phenomenon was occasionally observed in inland heaths where the water-table was near the surface; but in heath soils lacking vertical zonation, *M. ramannianus* was generally present at all depths sampled, and in podsolized soils its vertical distribution was sharply checked at the illuviated horizons. The low frequency of isolation of *M. ramannianus* from surface soils may have resulted from the vigorous competition of other species on plates prepared from these soils. Early excision, from soil plates, of fungi with a rapid and spreading growth habit did not, however, result in an increase in the number of *M. ramannianus* colonies.

Root isolation studies, employing a root washing device similar to that described by Simmonds[10], indicated that *M. ramannianus* was a common and active root-surface inhabitant. It occurred with frequencies of 25 per cent and 50 per cent on *Ammophila* roots from the A_1 and subsurface soils respectively in acid-fixed dunes, but was not recorded on such roots from the fore-dunes. The fungus was also very common on *Calluna* roots from the A_2 and B_1 horizons of an inland dry heath soil. Thrower[11], however, has concluded, from the studies of the rhizospheres of Australian heath plants, that *M. ramannianus* was predominantly an inhabitant of the free soil and infrequent in the root region.

Our investigations indicate that *M. ramannianus* is a prominent member of acid, semi-fixed and fixed dune heath and inland dry heath communities. Since it was isolated readily by a modified slidetrap method[12] from both types of habitat, it is probable that the fungus commonly exists as an active mycelium in these soils. The calcifuge habit of *M. ramannianus* was indicated by its intolerance of alkalinity in culture media, where growth and sporulation were at a maximum at *p*H 3–4 and sparse at *p*H 7 (Brown[7]) and by its absence from calcareous dune systems. A similar influence of hydrogen ion concentration on its growth has also been demonstrated by Müller[6]. The distribution of *M. ramannianus* in a wide range of heathland soils and its absence from wet dune lows and slacks indicated an intolerance also of damp soil conditions, or some other associated factor. (It should be noted that neither of these factors appears to be completely limiting since Stenton[13] isolated *M. ramannianus* from slightly alkaline, peaty soil at Wicken Fen.) Throughout the investigations there was no indication that the occurrence of *M. ramannianus* was related to the presence of illuviated horizons in the soil profiles, as has been suggested by Jefferys *et al.*[3] and McLennan and Ducker[4,5]; indeed, the results presented by Jefferys *et al.* may be interpreted in relation to soil moisture status (as judged by the nature of the surface flora) as readily as to the presence of a well-marked iron-pan in the *B* horizon.

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Perfect Stage of *Keratinomyces ajelloi*

Keratinomyces ajelloi was first described in 1952 by Vanbreuseghem[1], who isolated it from soil by means of a technique[2] which consists of placing hair on the surface of the soil in a Petri dish as 'bait' for keratinophilic fungi. Since this original isolation, the fungus has been reported many times and is clearly a common inhabitant of soil and of widespread distribution.

Recently, fourteen samples of soil from eight districts in Glasgow and the west of Scotland were investigated for keratinophilic fungi. *K. ajelloi*, in most cases with certain other keratinophilic fungi, was isolated from thirteen samples. The remaining sample did not contain any keratinophilic fungi.

The soil samples were collected into polythene bags from the top 4 in. of cultivated land or immediately beneath the turf of fallow land and processed within a few days. Essentially the technique employed was that of Vanbreuseghem; but the soil was baited with horse mane or tail hair, child's hair, shreds of cow horn and feathers, as well as with adult human hair. The Petri dishes were incubated at 28° C. and examined at intervals over a period of 5–6 weeks.

K. ajelloi could be identified by microscopic examination, and inoculations made for culture as early as one week after baiting. By the end of the

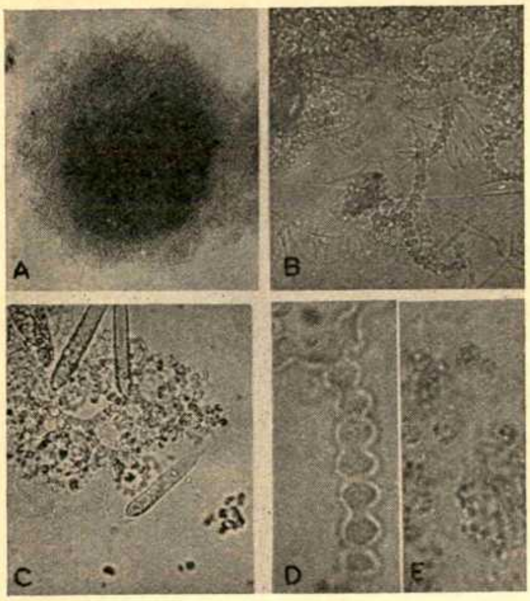

Fig. 1. *A*, mature cleistothecium, mount lactophenol (× 65); *B*, peridium showing characteristic branching and spiral appendages, mount cotton blue in lactophenol (× 265); *C*, macroconidium formed from peridial hyphæ, mount lactophenol (× 250); *D*, cells of peridial hyphæ (× 625); *E*, asci (× 625)

third week, creamy yellow globose structures had developed on certain of the baits on the surface of seven of the soil samples from three districts. Microscopic examination revealed these to be cleistothecia. They were closely associated with *K. ajelloi*, and it was shown by culture of complete cleistothecia and of single ascospores that they were in fact the perfect stage of this fungus. There was no evidence of sexual reproduction in the six isolates of *K. ajelloi* from the soil of the remaining four districts.

The cleistothecia (Fig. 1*A*), which measure 300μ–900μ in diameter, have a peridium of pale yellow hyphæ with a characteristic pattern of claw-like branches (Fig. 1*B*) entangled to form a close network. The individual cells (Fig. 1*D*) are dumb-bell shaped with thick echinulate walls and many of them bear long, smooth-walled spiral appendages (Fig. 1*B*) or occasionally macroconidia of the characteristic *Keratinomyces* form (Fig. 1*C*). The asci (Fig. 1*E*) which are formed in large numbers are sub-globose, and each contains eight bright yellow ascospores with finely echinulate walls.

Sexual reproduction is apparently influenced by a number of factors. It was never observed in culture on agar media, and on primary isolation cleistothecia were formed regularly on only certain of the keratinaceous baits. On horse hair and child's hair they were always produced abundantly, whereas on adult human hair on the same soils they formed sparsely on only one occasion after an incubation period of 6–8 weeks.

A number of attempts were made to ascertain the conditions necessary for sexual reproduction. Complete cleistothecia were inoculated on autoclaved horse hair which was maintained in a humid atmosphere; but a few cleistothecia were produced on only two of the many occasions on which this was done. Unsatisfactory results were also obtained from a large series of experiments in which sterilized soil previously inoculated with cleistothecia or with agar cultures was baited with horse hair. Eventually regular sexual reproduction on horse-hair bait was achieved by inoculation of unsterilized soil with cultures of cleistothecial strains. For this purpose the soil known to be negative for keratinophilic fungi was used. Attempts were then made to induce sexual reproduction in those strains which had not formed cleistothecia when isolated originally. They were inoculated singly and in combination with one another or with single ascospores strains into the unsterilized negative soil baited with horse hair. However, cleistothecia were never formed. Three single ascospore cultures (*A*, *B* and *C*) were also treated in this way. Cleistothecia formed regularly in all the Petri dishes inoculated with strain combinations *AB* and *AC* but not with combination *BC* or with single strains.

It would therefore appear that *K. ajelloi* is heterothallic and that compatible strains will reproduce sexually under certain conditions which are fulfilled by certain keratinaceous baits on the surface of unsterilized soil. However, certain strains may have lost their ability to reproduce by sexual means. In this small series it has been noted that those strains which were 'non-cleistothecial' on original isolation and in which cleistothecial formation could not be induced failed to produce the typical vinaceous red pigment when grown on glucose peptone agar. All cleistothecial strains formed pigment, as did the monospore cultures. There is, as yet, insufficient evidence to assume that pigment production is indicative of ability to reproduce sexually, but this and other aspects are being further investigated.

We are indebted to Mrs. E. Forbes for assistance with minospore isolations and to Miss E. Brown for technical assistance.

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Inactivation of Organo-Mercurial Fungicides in Groundwood Pulp made from Logs stored in Salt Water, and the Possible Role of Sulphur Compounds

RECENT experiments conducted in our laboratories have shown that there is a correlation between the efficiency of organo-mercurial fungicides, used for the preservation of moist groundwood, and the concentration of certain sulphur compounds in the logs from which the groundwood is produced. These sulphur compounds are considered to arise from the reduction of inorganic sulphates, absorbed from salt or brackish water during storage, by halophilic strains of *Desulphovibrio desulphuricans*. These bacteria have been isolated from the sapwood of logs stored under natural conditions in sea water for a year. Chemical and microbiological studies have been made on samples of pulp, and on logs obtained from a number of Scandinavian groundwood mills after storing for different periods in fresh water, brackish water and sea water. In every case high sulphur contents, expressed as sulphidic and reducible[1] sulphur, were found both in pulp samples containing biologically inactive fungicide and in the sapwood of the logs from which they had been made. Conversely, pulps having a high residual content of biologically active fungicide (and consequently a good record of freedom from fungal infection during storage) contained considerably less sulphidic and reducible sulphur, as did the corresponding logs. The latter logs and groundwood pulps came from mills where the wood is stored for 1–2 years in fresh water prior to grinding; the former from mills on or near the coast where the logs are kept in sea water or brackish water for similar periods of time. It has, in fact, been found that after only three months soaking of logs in sea water, mercurial fungicides are de-activated at once on addition to the resultant pulp. It has been shown in the laboratory that the de-activating property progresses farther into the heart of the log with increasing length of immersion.

(In this work sulphidic sulphur has been defined as hydrogen sulphide liberated by hydrochloric acid, and reducible sulphur as sulphur present in the sample and reducible, under the conditions of test, to hydrogen sulphide.)

Sea water itself has been shown to have no adverse effect on either phenyl mercuric acetate or phenyl mercuric acetate-8-hydroxyquinoline (P.M.A.-oxine) mixtures. Thus, from these observations and the presence of *D. desulphuricans*, the inference may be drawn that the absorption by logs of inorganic sulphates is followed by reduction to certain sulphur compounds, which are able to bring about the formation of biologically inactive mercury compounds when the fungicide is added to the pulp. The interaction between mercury and its salts and hydrogen sulphide produced in soil by the bacterial reduction of sulphates has been reported by Booer[2]. Whatever the precise mechanism of this final step may be, the de-activating effect has been found to be immediate with both commercial and laboratory-made pulps derived from sea water-soaked logs.

The exact forms in which these sulphidic and reducible sulphur compounds are present in the wood (or pulp) is still being investigated; it is possible that hydrogen sulphide liberated by bacteria may react to form thiolignin[3] and this point is under investigation.

A detailed account of this work will eventually be published elsewhere.

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GENETICS

Stable Equilibrium at a Sex-linked Locus

Bennett[1] has shown that a stable selectively balanced polymorphism between two alleles can exist at a locus in the X-chromosome under conditions which are different from those determining stable equilibrium in the autosomal situation. In particular, it is neither necessary nor sufficient, in the sex-linked case, for the heterozygote in the homogametic sex to be at a selective advantage with respect to both homozygotes. It has previously been found[2] that this principle of heterozygosity operates in the case of multiple allelic systems in autosomes in the following form: a necessary condition for stable equilibrium is that the viability of each homozygote be less than the mean viability of the zygotic population at equilibrium. It seems at first sight that no such heterozygosity principle operates in the sex-linked situation. It will, however, be shown here that it does do so in a somewhat modified form.

It is convenient here to use homogeneous parameters to express relative viabilities, rather than Bennett's method of expressing them relative to the viability of the heterozygote. Thus we may have, for two alleles A,B (taking females as the homogametic sex):

	Females			Males	
Genotype Relative viability	AA a	AB h	BB b	A a^*	B b^*

In any one generation let the frequencies of A,B be p,q respectively in females, and p^*,q^* respectively in males, so that:

$$p + q = 1, \quad p^* + q^* = 1 \tag{1}$$

Then in the next generation (after random mating) we obtain genotypic frequencies as follows:

	Females			Males	
Genotype	AA	AB	BB	A	B
Frequency before selection (zygotes)	pp^*	$pq^* + p^*q$	qq^*	p	q
Frequency after selection (mature adults)	$\frac{app^*}{T}$	$\frac{h(pq^* + p^*q)}{T}$	$\frac{bqq^*}{T}$	$\frac{a^*p}{T^*}$	$\frac{b^*q}{T^*}$

$$\left.\begin{aligned} \text{where } T &= app^* + h(pq^* + p^*q) + bqq^* \\ T^* &= a^*p + b^*q \end{aligned}\right\} \tag{2}$$

For equilibrium of the gene frequencies in the two sexes the gene ratios must have the values:

$$\text{in females: } R = \frac{p}{q} = \frac{h(a^* + b^*) - 2bb^*}{h(a^* + b^*) - 2aa^*} \tag{3}$$

$$\text{in males: } R^* = \frac{p^*}{q^*} = \frac{a^*}{b^*} R \tag{4}$$

Moreover, the equilibrium is stable if and only if the conditions:

$$\frac{h(a^* + b^*)}{2} > aa^*, \quad \frac{h(a^* + b^*)}{2} > bb^* \tag{5}$$

are satisfied.

It is clear from (3) and (5) that for the homogametic sex the conditions determining equilibrium and its stability are identical with those governing two alleles A,B at an autosomal locus in which the relative viabilities of the genotypes AA, AB, BB are

$$a' = aa^*, \quad h' = \frac{h(a^* + b^*)}{2}, \quad b' = bb^* \text{ respectively.}$$

If we now consider females only with the modified relative viabilities a', h', b', the principle of heterozygosity emerges in the following way. The mean viability V_e of female zygotes at equilibrium can be written:

$$V_e = a'pp^* + h'(pq^* + p^*q) + b'qq^* \tag{6}$$

where p, q, p^*, q^* satisfy (1), (2) and (3).

Now,

$$V_e = a' + \left\{(b' - a') + (h' - a')R\left(1 + \frac{a^*}{b^*}\right)\right\}qq^*$$
$$= a' + \left\{(h' - a') + \frac{a^*}{b^*}(h' - b')\right\}qq^*$$

using (2) and (3).

If the equilibrium is stable then (5) holds also and we have:

$$V_e > a' = aa^* \qquad (7)$$

and similarly: $V_e > b' = bb^*$ (8)

These conditions are necessary for the existence of a stable equilibrium, and constitute the heterozygosity principle in its modified form.

It is worth while noting a second form of the new heterozygosity principle which in the case of an autosomal allelic system has proved a valuable interpretative guide. In the present case the second form of the principle is entirely equivalent to either of the formulations given above, namely, (i) $h' > a', b'$; (ii) $V_e > a', b'$.

If in the mature females the genotypic frequencies of AA, AB and BB are u, v and w respectively, then under random mating without selection the index:

$$\varphi = \frac{v^2 - 4uw}{(2u + v)(v + 2w)} \qquad (9)$$

(which is in fact minus the inbreeding coefficient F) is zero.

In the polymorphism considered here, φ is equal to a positive multiple of:

$$h^2(R + R^*)^2 - 4abRR^* = R^2\left\{h^2\left(1 + \frac{a^*}{b^*}\right)^2 - 4ab\frac{a^*}{b^*}\right\}$$
$$= \frac{4R^2}{b^{*2}}\left\{h'^2 - a'b'\right\}$$

and this is positive by the conditions (5) for stability. This indicates that a condition for stability is that the female heterozygotes are present in excess of Hardy–Weinberg expectations. Thus the principle of heterozygosity holds in this case in a very definite and graphic form.

The above treatment of a sex-linked locus in terms of the autosomal case can be extended to multi-allelic loci in the X-chromosome. This will be discussed elsewhere.

I wish to thank Dr. A. R. G. Owen for suggesting this problem and for much helpful advice and encouragement; and the Royal Commission for the Exhibition of 1851 for the award of an Overseas Science Research Scholarship.

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Congenital Transmission of Toxoplasmosis through Successive Generations of Mice

CONGENITAL transmission of infectious agents—viruses, rickettsiæ, spirochætes and piroplasms—is not uncommon in arthropods and may pass through many generations. It is much less common in mammals in which, when it occurs, it usually stops at the second generation. In mice, however, the virus of lymphocytic chorio-meningitis can be transmitted indefinitely[1], and there are claims that in man syphilis can pass to the third generation[2].

The protozoon *Toxoplasma* was reported by Wildfuhr[3] to have been congenitally transmitted to the third generation of rats. Recently, I have observed its transmission to successive generations of mice—five so far.

The experiments started with infection by subcutaneous inoculation of Swiss mice, six between the eighth and sixteenth days of pregnancy, one 2 days after a mating, which did not result in obvious pregnancy, and one 5 days after delivery. The inoculation consisted of between 30 and 600 cysts of a strain of *Toxoplasma* of low virulence (rabbit A), originally isolated from a naturally infected, but apparently healthy, laboratory rabbit. Although congenital infection with the strain shortens the lives of mice, reduces the number of litters they produce and the number reared to maturity in each litter, artificial inoculation does not make them obviously sick unless done during pregnancy or lactation. To this may be ascribed the heavy mortality in most of the first litters of the original mice, as a result of which in only one of these did a female survive to continue the line. In the other instances the lines derived from second litters.

All eight mice transmitted *Toxoplasma* infection to some of the second generation. Two lines of infection stopped there; one because the only infected female of the second generation proved infertile and the other because the one surviving female was killed when a very low antibody titre was, erroneously, taken to signify absence of infection. Four continued to the third generation at which one stopped because only males were infected and two because the females did not become pregnant. The fourth still goes on. Also continuing, and infected, are one line in the fourth and one in the fifth generations.

In all there have been 33 first or subsequent pregnancies in the original mice or their descendants. Except in three of these pregnancies, some of (on average half) the litter have been infected.

The presence of infection in a litter was determined by killing the males when 6 weeks old, making emulsions of their brains and examining them for *Toxoplasma* cysts. If these were found, the females were reared for a further 4 weeks and then mated to non-infected males. Before this their blood serum was in some instances examined for *Toxoplasma* antibodies, and when they were eventually killed all their brains were examined for cysts.

It would seem likely that infection is transmitted, for the most part, before birth, for toxoplasms were isolated by inoculation of surgically removed fœtuses into uninfected mice.

Of course it can also be transmitted by the milk, as shown by Eichenwald[4]. This I can confirm as the result of experiments in which mice were inoculated during lactation. Infection does not appear to be transmitted by droplet, fæces, urine or by copulation, for 10 female mice and their 33 litters, comprising 216 offspring, did not acquire infection from 10 infected males with which they were caged for 4–8 months.

There are many puzzling features in *Toxoplasma* infection of laboratory mice. Natural infection is fortunately almost unknown, yet mice are very susceptible to inoculation, to intranasal instillation of proliferative forms, or to feeding with cysts. Cannibalism is the only way yet known by which adult mice can be infected naturally, yet when infection is established it passes fairly readily from generation to generation. Nor is it necessary, as Eichenwald[4] believed, for infection to be recent and acute. Twenty-three of the infected litters were borne of mothers themselves congenitally infected, and in one instance a congenitally infected mother produced congenitally infected offspring even in her fourth litter.

J. K. A. BEVERLEY

Department of Bacteriology,
University of Sheffield.
Feb. 9.

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[2] Nabarro, O., "Congenital Syphilis" (Arnold, London, 1954). Szego, L., *Dermatol. Wschr.*, **133**, 560 (1956).

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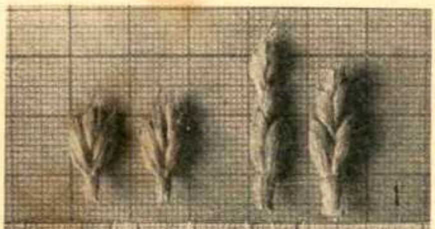
An Induced Mutant in *Triticum carthlicum* with the Diagnostic Feature of *T. vavilovi*

THE spike of *Triticum vavilovi* Jakub. is distinctive in that the internodes of the rachilla are more elongate and the number of rachilla nodes increased compared with other hexaploid wheats. The elongated rachilla internodes sometimes so reduce the extent to which the florets overlap as to give the spikelet two or three distinct levels (Fig. 1).



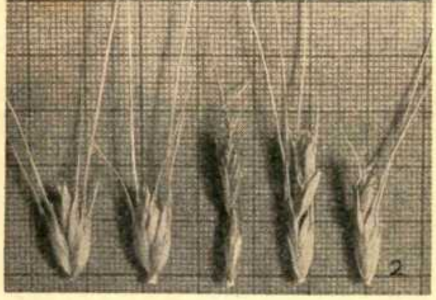


Fig. 1. Two *T. aestivum* normal (left) and two *T. vavilovi* spikelets with several levels (right)

Fig. 2. Two *T. carthlicum* normal (left) and three *T. carthlicum* mutant spikelets (right) with several levels

In 1955, as part of a larger programme, dry seed of genetically pure *T. carthlicum* Nevski (= *T. persicum* Vav.), a tetraploid wheat, was treated with a dose of 10,000 r. X-rays. In the X_3 generation, examined in 1957, a mutant was found which strikingly resembled *T. vavilovi* (Fig. 2). This type had not been present in the X_1 or X_2 generations, but 21 plants in the X_4 progeny of the mutant plant all repeated the mutant structure.

The most important divergences of this mutant from the original *T. carthlicum* stock are compared in Table 1 with the differences between *T. vavilovi* and *T. aestivum* var. Newthatch, the hexaploid common wheat. The total extent of the difference between the *T. carthlicum* mutant and the parental stock is readily ascertainable but the extent of the original difference between *T. vavilovi* and *T. aestivum* cannot be exactly determined because of the present variation in the latter species. The two species are constantly differentiated only by the characters listed in Table 1. Many of the spikelet types seen in the investigation of the genetical constitution of *T. vavilovi* by Singh, Anderson and Pal[1] were observed in this relatively small range of mutant material.

Table 1

Character	Hexaploids		Tetraploids	
	T. aestivum	*T. vavilovi*	*T. carthlicum*	Mutant
Spike	normal	pseudo branch	normal	pseudo branch
Spikelet number of levels	1	2, sometimes 3	1	2, sometimes 3
Rachis at the spikelet bases			glabrous	pubescent
Rachilla number of nodes	5	7	5	7
Internodes	short	elongated	short	elongated
Glume, outer glume			bearded	beardless, with beak-shaped end
Inner glume, arista			long	shorter

According to Isenbeck and Rosentiel[2], Vavilov does not touch upon the genetical bases of *T. vavilovi*. Isenbeck and Rosentiel suggest that the development of this form may be explained as a one-step mutation from *T. aestivum*. This explanation is not excluded by the data of Singh, Anderson and Pal[1] from crosses between *T. vavilovi* and several *Triticum* species. Further, it appears that there is no genome difference between *T. aestivum* and *T. vavilovi*. This hypothesis is confirmed, at the tetraploid level, by a mutant analogous with *T. vavilovi* which actually originated in a single mutational step. In this case of parallel mutations, it may be supposed that since the final outcome was identical the pathways were also identical.

The genetic foundations of the mutant in *T. carthlicum* will only be established by crossing experiments already commenced. The mutation of a single gene to the recessive condition would be the most simple explanation for segregation occurring in X_3 and for the mutant to be true breeding in X_4.

Summing up, the 'vavilovoid' mutant may be of interest in that it illustrates parallel variation and parallel genotypes at the tetraploid and hexaploid level. Moreover, it throws light on the origin of *T. vavilovi* and confirms the supposition of Isenbeck and Rosentiel. Finally, it raises a taxonomic problem, namely, that if *T. vavilovi* is treated as a distinct species as classified by Vavilov[3], by Jakubsiner[3] and by Singh, Anderson and Pal[1], then it must be accepted, at the tetraploid level, that a new species arose from *T. carthlicum* in a single mutational step. Alternatively, if *T. vavilovi* is treated as a subspecies of *T. aestivum*, as it is classed by Sears[4] and by Schiemann[4], subspecific variation must have originated in a single step.

Z. BARABÁS, JUN.

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Nov. 24.

[1] Singh, H. B., Anderson, E., and Pal, B. P., *Agron. J.*, **49**, 4 (1957).

[2] Isenbeck, K., and Rosentiel, K., "Handbuch der Pflanzenzüchtung", **2**, 289 (Parey, Berlin and Hamburg, 1950).

[3] Vavilov, N. I., "The Origin, Variation, Immunity and Breeding of Cultivated Plants", **13**, 364 (Chronica Botanica, 1949–50).

[4] Sears, E. R., "Handbuch der Pflanzenzüchtung", **2**, 164 (Parey, Berlin and Hamburg, 1956).

FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Monday, May 11

University of London (at the Royal Veterinary College, Royal College Street, London, N.W.1), at 5 p.m.—Dr. G. C. Ainsworth: "The Fungus".* (First of three Special University Lectures on Fungous Diseases of Animals". Further lectures on May 12 and 14.)

University of London (at the Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London, W.2), at 5 p.m.—Prof. G. W. Beadle (California Institute of Technology): "The Molecular Basis of Heredity".* (Last of a series of four Almroth Wright Lectures.)

University of London (in the Physiology Theatre, University College, Gower Street, London, W.C.1), at 5 p.m.—Dr. J. B. Neilands (California): "Iron Metabolism in Micro-organisms".*

British Society for the Philosophy of Science (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Mr. G. Gorer: "The Concept of National Character".

Royal Institution, Library Circle (at 21 Albemarle Street, London, W.1), at 5.30 p.m.—Dr. H. Lowery: "Gilbert White and His 'Natural History of Selbourne' ".

Institution of Electrical Engineers, Education Discussion Circle (at Savoy Place, London, W.C.2), at 6 p.m.—Discussion on "Trends in the Teaching of Electric Machine Theory in the United States", opened by Mr. P. L. Alger.

Royal Geographical Society (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Mr. Eric Shipton, C.B.E.: "Explorations in Patagonia".

Monday, May 11—Wednesday, May 13

Institution of Chemical Engineers; Society of Instrument Technology; and the British Computer Society (at the Central Hall, Westminster, London, S.W.1)—Joint Symposium on "Instrumentation and Computation in Process Development and Plant Design".

Tuesday, May 12

Society of Chemical Industry, Agriculture Group (at 14 Belgrave Square, London, S.W.1), at 10.30 a.m.—Annual General Meeting, followed by a full-day Meeting on "The Manuring of Tropical Crops".

University of London (at the London School of Economics and Political Science, Houghton Street, Aldwych, London, W.C.2), at 5 p.m.—Dr. Frederick Barth (Oslo): "The Anthropological Study of Middle Eastern Societies".*

University of London (at the Royal Veterinary College, Royal College Street, London, N.W.1), at 5 p.m.—Dr. G. C. Ainsworth: "The Fungus and the Host".* (Second of three Special University Lectures of "Fungous Diseases of Animals". Further lecture on May 14.)

University of London (in the Physiology Lecture Theatre, Guy's Hospital Medical School, London Bridge, S.E.1), at 5 p.m.—Sir George Thomson, F.R.S.: "The Principles of Physics" (Fison Memorial Lecture).

Zoological Society of London (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

Parliamentary and Scientific Committee, General Committee (in the Grand Committee Room, Westminster Hall, House of Commons, S.W.1), at 5.30 p.m.—Discussion on "Modern Techniques and their Application to and Influence on New Buildings" opened by Mr. Norman Wates and Mr. Anthony Pott.

Society of Chemical Industry, Chemical Engineering Group (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Mr. W. Quick: "Fuel Economy in Chemical Works".

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Prof. J. D. Evans: "The Animal World of Prehistoric Farmers and Pastoralists in Europe".* (Second of six lectures on "Animals in Archæology". Further lectures on May 19, 26, June 2 and 9.)

British Computer Society (at the Northampton College of Advanced Technology, St. John Street, London, E.C.1), at 6.15 p.m.—Mr. T. C. Hickman: "Early Experience with an E. D. P. Installation".

Pharmaceutical Society of Great Britain (at 17 Bloomsbury Square, London, W.C.1), at 7.30 p.m.—Mr. N. J. Van Abbe: "Pharmaceutical Aspects of Dermatological Treatment".

Wednesday, May 13

University of London (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 2 p.m.—Dr. E. F. Gale: "Disorganization of the Bacterial Cell by Antibiotics".*

Royal Meteorological Society (at 49 Cromwell Road, London, S.W.7), from 2.30 p.m.–6 p.m.—Discussion on "The Dynamics of Cumulonimbus". Opening Speakers: Dr. R. S. Scorer, Mr. P. M. Saunders, Mr. F. H. Ludlam and Mr. W. G. Harper.

Geological Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. F. Dixey: "The Geomorphology of Madagascar".

Linnean Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. Hans Helbaek (Copenhagen): "Archæology and the Evolution of the Cultivated Plants, with special reference to *Linum*".

University of London (at the Institute of Diseases of the Chest, Brompton Hospital, London, S.W.3), at 5 p.m.—Dr. R. W. Riddell: "Aspergilli as a Cause of Pulmonary Disorders".*

Institution of Electrical Engineers, Radio and Telecommunication Section (at Savoy Place, London, W.C.2), at 5.30 p.m.—Mr. E. G. Rowe: "The Application of Statistical Techniques to the Electric Valve Industry".

Society of Chemical Industry, Food Group (at 14 Belgrave Square, London, S.W.1), at 6 p.m.—Scientific Papers (Seventh Young Members' Meeting).

Society of Instrument Technology, Data Processing Section (at Manson House, Portland Place, London, W.1), at 6 p.m.—Annual General Meeting, followed by Mr. J. R. Sturgeon: "A Multipoint Digital Strain-Gauge Recorder".

British Institution of Radio Engineers (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 6.30 p.m.—Prof. D. Gabor, F.R.S.: "Improving Communication Techniques—What Have Engineers to Learn from Information Theory ?".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. G. Kitson Clark: "The Modern State and Modern Society: Historic Tendencies and Future Probabilities".

Thursday, May 14

Association of Agriculture (at 53 Victoria Street, London, S.W.1), at 11.30 a.m.—Annual General Meeting.

University of London (at the Royal Veterinary College, Royal College Street, London, N.W.1), at 5 p.m.—Dr. G. C. Ainsworth: "The Fungus, the Host, and the Environment".* (Last of three Special University Lectures on "Fungous Diseases of Animals".)

Institution of Electrical Engineers (at Savoy Place, London, W.C.2), at 5.30 p.m.—Annual General Meeting. 6.30 p.m.—Prof. E. C. Cherry: "On the Conceivable Future of Telecommunications".

Royal Aeronautical Society (at the Institution of Mechanical Engineers, Birdcage Walk, London, S.W.1), at 6 p.m.—Mr. C. J. McCarthy: 47th Wilbur Wright Memorial Lecture.

Institute of Biology (at Brunel College of Technology, Woodlands Avenue, Acton, London, W.3), at 7.30 p.m.—Dr. L. G. C. E. Pugh: "Men at High Altitudes".*

Friday, May 15

Institute of Navigation (at the Royal Geographical Society, 1 Kensington Gore, London, S.W.7), at 5.15 p.m.—Captain E. G. Irving, O.B.E., R.N.: "Electronic Surveys in the Caribbean".

Society of Chemical Industry, Fine Chemicals Group (at 14 Belgrave Square, London, S.W.1), at 6.30 p.m.—Annual General Meeting. 7 p.m.—Dr. H. T. Openshaw: "New Developments in the Chemistry of Emetine and Related Alkaloids".

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Assistant Librarian (with a good honours degree and experience in an academic library)—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (May 16).

Lecturer and an Assistant Lecturer in the Department of Physics—The Registrar, The University, Nottingham (May 16).

Lecturer or Assistant Lecturer (with a good honours degree in physics) in Physics—The Dean, Guy's Hospital Medical School, London Bridge, London, S.E.1 (May 21).

Assistant Lecturer in Geography—The Registrar, The University, Sheffield (May 23).

Assistant Lecturer or Lecturer (preferably with interests in applied mathematics) in the Department of Mathematics; and a Temporary Assistant Lecturer or Temporary Lecturer (preferably with interests in applied mathematics) in the Department of Mathematics—The Secretary, University College, Gower Street, London, W.C.1 (June 1).

Lecturer (preferably with an interest and experience in the field of electrical machinery) in Electrical Engineering—The Deputy Registrar, The University, Birmingham 15 (June 1).

Assistant Experimental Officer (with a degree in a biological subject and practical experience in bacteriological methods and techniques) for work on the ecology of soil micro-organisms—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (June 30).

Senior Lecturer in Mathematics at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, (June 30).

Chair of Engineering—The Registrar, The University, Leicester.

Senior Lecturer (with good academic qualifications, teaching experience and preferably special qualifications or experience in mathematical statistics or other branch of applied mathematics) in Mathematics—The Registrar, Hatfield Technical College, Hatfield.

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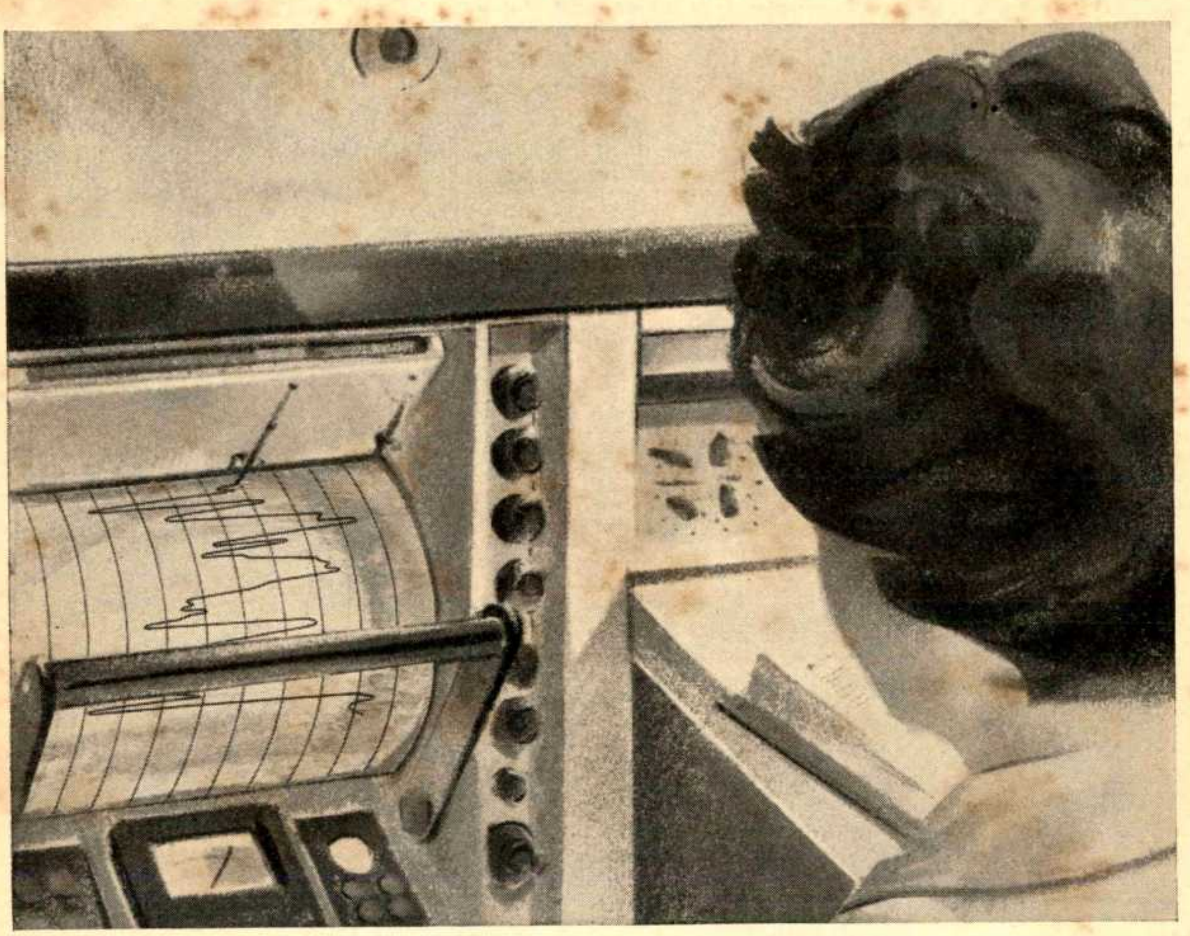

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* *G. B. B. M. Sutherland and H. W. Thompson, Faraday Society Transaction*, 41 175 1945.

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NUCLEAR DISARMAMENT

IT would be an exaggeration to describe the debate on nuclear disarmament in the House of Lords on February 11 as a dissertation on Lord Russell's book*, but seldom have so many speakers in a debate referred so freely to a single book. The motion under debate was primarily concerned to discourage further Powers from manufacturing or owning nuclear weapons, and to this end Lord Simon of Wythenshawe proposed that Britain should cease herself to manufacture nuclear weapons and should destroy her stocks, provided other industrial nations except the United States and the U.S.S.R. themselves undertook not to own, manufacture or use such weapons. The United Nations would be asked to accept responsibility for inspection and enforcement, and the United States and the U.S.S.R. would be urged to help the United Nations and to undertake not to supply nuclear weapons to another country.

Lord Russell himself supported the motion, but put it in the larger context which his book supplies, and stressed the tendency to under-estimate the evils that would result from a really serious nuclear war. That is the starting point of his argument: these evils are so great that national self-interest itself demands the avoidance of nuclear war. A large-scale nuclear war would be an utter disaster to all mankind, including the belligerents, and would achieve no result that any sane man could desire. There is, moreover, considerable risk that a small war may develop into a great war, and even if existing nuclear weapons had been destroyed and there were an agreement that no new ones should be manufactured, any serious war would become a nuclear war as soon as the belligerents had been able to manufacture the forbidden weapons.

Thus far, Lord Russell can fairly claim to be writing common sense on nuclear warfare, though experience in regard to gas warfare seems to invalidate his last point. It was, nevertheless, made in the Vienna Declaration adopted by the participants in the Third Pugwash Conference at Kitzbuhel and Vienna in September 1958, as was noted in the debate in the House of Lords, and it must be conceded as a possibility. The instinct to survive could lead any nation to disregard any agreement or undertaking, even when the common interest of survival as well as the desire to escape from the crushing burden of the arms race make the elimination of war a matter of plain self-interest.

While, however, Lord Russell writes very cogently and reasonably about the steps to be taken towards peace and the new outlook needed before negotiations can hope to succeed, reason sometimes fails to take account of realities, not to mention difficulties. He believes that impartial agreements could be reached once both sides recognize that it is more important to reach agreement than to win diplomatic victories, and he sees some hope in the reduction of vituperation, though he points out also that propaganda should increasingly be directed to the promotion of the awareness of common humanity. He stresses the importance of government agreement on the abolition of nuclear tests as a first step towards peace, and with the resumption on April 13 of the Geneva conference on ending nuclear tests it should soon be clear how far both sides truly desire agreement. Mr. Selwyn Lloyd's reply in the House of Commons on April 15 indicates that an attempt is being made to meet the Russian objections to inspection by international teams and to utilize the opportunity which a system of control by 180 static posts might offer. The U.S.S.R. is already prepared to accept the manning of five of the ten key positions in each static post by nations of the other side, and the Western view is that one-third of the key posts should be filled by staff from the three nuclear powers and the remainder filled by the host country.

The difference between a demand for five and one for six or seven does not seem wide, but Lord Russell's second step is less simple. He suggests that the next step should be a solemn joint declaration by the United States and Soviet Russia to the effect that they will seek to settle their differences otherwise than by war or the threat of war, and that to implement this declaration they should appoint a permanent joint body to seek measures tending towards peace and not altering the existing balance of power. Lord Russell suggests that this body should be invited to study every dispute that might arise, and to suggest such settlements as each side might be willing to accept.

Nowhere, however, does Lord Russell indicate precisely what advantage such a body would offer over those already in being, given indeed the new outlook that he commends, which indeed is essentially a re-appraisal of what national interests really involve. Moreover, the problems to come before the new body are essentially questions of disarmament and territorial questions. On the former, Lord Russell adds nothing new and points out that disarmament is really a palliative rather than a solution of the problem of world order—rather a sequence of improved international relations than a cause of better relations. The actual steps towards conciliation which he proposes, however, seem to ignore the real difficulties and, to say the least, in suggesting the appointment of a conciliation committee to explore measures for diminishing tension, it is more than a little naïve to suggest that all policy makers in the modern world are too busy to acquaint themselves with the facts upon which policy should be based. On territorial adjustments, he observes that the countries of Europe should be freed from alien forces and their immunity guaranteed, but he does not indicate by whom, though he is realistic enough to regard the withdrawal of American forces from

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* Common Sense and Nuclear Warfare. By Bertrand Russell. Pp. 94. (London: George Allen and Unwin, Ltd., 1959.) Cloth, 7s. 6d.; Paper, 3s. 6d.

Western Europe as impracticable save as a sequel to an enforceable agreement for abolishing nuclear weapons. Applied to the Far East, his suggestions completely disregard his own principle of respecting the wishes of the inhabitants and we are given no clue as to how friction, uncertainty and rivalry in difficult regions can be eliminated or by whom an international authority with power to enforce its decisions could be created. Indeed, Lord Russell admits that for the present this is an academic creation and appears to visualize it as developing from a series of subordinate federations in such a federal world as Lord Curtis advocates. Ultimately, his hope seems to rest on education and in the policies he outlined in an earlier book, "New Hopes for a Changing World". Here he gives us little clue as to how hope is to be substituted for fear and the co-operation secured on which world order and security can ultimately be based.

The Earl of Dundee, replying for the Government on the debate on February 11, affirmed that the right solution was disarmament by agreement, and collective security under a world system which commands the confidence and assent of all nations ; but he did not suggest that this could be achieved other than by patience and perseverance. He did not believe that it is possible to establish a system of world society in which conventional wars are still allowed but nuclear wars are excluded, and agreed with Lord Russell both that all future wars would be nuclear and that the Russian phobia about inspection is the real obstacle. He pointed out that Lord Russell had not really indicated what different method and new approach should be adopted, but in stressing the importance of a continued attempt to break down the cultural and intellectual barriers of the Iron Curtain and to establish real freedom of intercourse between the leaders of education, industry and science, between ordinary travellers and tourists, as well as the abolition of censorship, Lord Dundee went far towards accepting all that was constructive in Lord Russell's argument.

For the rest, the debate brought a further plea from Lord Boyd-Orr for world co-operation in applying the new powers of modern science to constructive purposes in the creation of a world free from war, hunger and preventable disease ; but Lord Adrian, who also supported Lord Simon's motion, merely emphasized the danger of allowing a nuclear war to start and the importance of preventing an increase in the number of Powers capable of starting such a war, without himself indicating any constructive steps to that end. Eventually, Mr. Selwyn Lloyd, Secretary of State for Foreign Affairs, in reply to questions in the House of Commons on April 15, said that the Government had proposed to the resumed Geneva Conference on nuclear tests that, if the Soviet Union could not agree to the steps required to make a comprehensive ban possible, attempts should be made to reach such a ban by stages.

The first stage would consist of a ban on tests from the Earth's surface up to 50 kilometres and under-water tests. Agreement on controls for this purpose seemed to be feasible, since on-site inspection would not be necessary. Efforts to work out the technical problems in detecting tests underground and at very high altitudes would continue without interruption, and as soon as satisfactory control provisions covering these points had been agreed and incorporated in the treaty tests in these environments would also be forbidden. Mr. Lloyd repeated that the Government would much prefer a comprehensive agreement but would accept the discontinuance of atmospheric tests as a first step and agree to negotiate further on the stopping of underground and stratospheric tests. (This has, of course, since been rejected.) Unlimited inspection had never been urged, but he thought that any control system is impossible if there is to be a Soviet veto on whether a complaint should be made and whether any alleged complaint should be inspected.

Lord Boyd-Orr's ideas concerning the importance of changing from the age-long use of war as the ultimate instrument of diplomacy to a new era of world peace, in which differences between nations will be settled by reason and goodwill, were more fully outlined in the presidential address he delivered to the Assembly of Corresponding Societies on August 28, 1958, at the Glasgow meeting of the British Association. Lord Boyd-Orr referred there to the economic and social problems which the great increase in the capacity for production of the modern world has created for the fully industrialized as well as for the underdeveloped countries ; but it was with the educational issues that his address was mainly concerned, particularly the education of the general public. He went so far as to suggest that what is needed to-day is a world-wide association for the retardation of science and for the preservation and increase of what culture we have available for dealing with the forces released by science.

In thus referring to the potential cultural value of the Assembly of Corresponding Societies, Lord Boyd-Orr was clearly referring to knowledge, wisdom and goodwill. It is obvious that we have still far to go before the Iron Curtain is no longer a barrier even in such fields ; but all measures to encourage cultural, educational and scientific exchange between the U.S.S.R. and the West could work to that end, and if the education of the public on the advancement of science and its impact on society become, as he suggests, the main function of the British Association, that Association might make an important contribution to world understanding. Meanwhile, an article by Prof. P. M. S. Blackett in *The Advancement of Science* (No. 60, March 1959) shows that the Association as a whole is making good progress in its new activities in presenting science to the public.

The Vienna Declaration of September 19, 1958, already noted, concluded by affirming the responsibility of scientists in all countries to contribute to the education of the peoples by spreading among them a wide understanding of the dangers and potentialities offered by the unprecedented growth of sciences. The Pugwash scientists appealed to their colleagues everywhere to contribute to this effort, both through enlightenment of the adult populations and through education of the coming generations. Both Lord Boyd-Orr's address and Prof. Blackett's article show that in Britain the British Association is already addressing itself to both aspects of the problem; but if scientists possess the special competence and responsibility attributed to them in the Vienna Declaration, these efforts will also require sustained support and constructive thought by professional associations of all kinds.

CORRESPONDENCE OF SIR JOSEPH BANKS

The Banks Letters

A Calendar of the Manuscript Correspondence of Sir Joseph Banks preserved in the British Museum, the British Museum (Natural History) and other collections in Great Britain. Edited by Warren R. Dawson. Pp. xlii + 965. (London: British Museum (Natural History), 1958.) £12 12s.

DURING the long reign of George III (1760–1820), and especially in the latter part, Sir Joseph Banks (1743–1820) was outstanding as the leader of scientific thought and development in Great Britain, above all in the realm of natural history in the widest sense. His great range of interests, his energy, his wealth, and his long term as president of the Royal Society, from 1778 until his death, enabled him to keep in close touch with the many and varied scientific activities of the period. Much has been written about Sir Joseph Banks but no full account of his voluminous correspondence and papers had been published, or even prepared, when they were largely dispersed, in part overseas, by sales in 1884 and 1886. The present volume is described as a Calendar and is concerned only with letters (originals or accepted *bona fide* copies) now in Britain. The extensive collections in other countries, especially in Australia, and the numerous reports, memoranda, or dissertations, mostly in his own handwriting, are not included. The letters listed with entries are now in the possession of many institutions and private persons, but the main collections are in the Department of Manuscripts of the British Museum, the Department of Botany of the British Museum (Natural History), and the Royal Botanic Gardens, Kew.

The Calendar as prepared and edited is arranged alphabetically on the basis of the names of the persons by whom or to whom the letters were written, and the letters are in order of date under the personal names, except for undated letters. For every letter there is given a concise epitome of its contents. So far as they have been traced, the dates of birth and death of the correspondents and an indication of their identity are given. Some idea of the magnitude of Banks's correspondence is given by the fact that the present Calendar contains entries of rather more than 7,000 letters and by the estimate that had the correspondence been intact the total would probably have been in the region of 50,000 or more. One has to remember that handwriting alone was involved, for in those days there were no typewriters or other modern devices for recording material not immediately to be published.

The work of reading and preparing explicit, if brief, entries of the contents of more than 7,000 letters must have been very considerable. The entries are well prepared and throw a great deal of light not only on the numerous and varied interests of Sir Joseph Banks and on the history of science in mid-Hanoverian times, but also on the conditions of life in Britain and other countries at this period. The basic alphabetical arrangement makes it easy to consult the entries and an excellent index enables the reader to make quick reference to subject contents.

In a short notice of a work of this nature and size it is impossible to do more than give general impressions of the range and value of the contents. As a source-book or a guide to sources for many purposes it will have considerable value. The historian of science, or of almost any branch of science, will frequently have to consult it, but many entries record matters outside the field of science. Indeed, it is the great range of Banks's interests and involvements which strikes one most in perusing the pages of this book. As Sir Gavin de Beer says in the preface he has written for the volume, "There is scarcely an aspect of British public life in the reign of George III that is not represented at first hand in the Correspondence of Sir Joseph Banks". He was certainly a remarkable man, and a great many institutions and individuals benefited from his advice and his often very concrete help. The British Museum, the Royal Botanic Gardens, Kew, and the Royal Society owe him a great debt, while many of the entries record thanks for kindnesses to individual correspondents.

It is appropriate that the present volume should be published by the Trustees of the British Museum. Not only did Banks contribute so much to the collections, particularly to those now at South Kensington, and a considerable part of the correspondence recorded in the body of the book is the property of the Museum, but also the work was originally initiated by the editor and the late Mr. John Ardagh, who was then in charge of the Library in the Department of Botany where the valuable Dawson Turner copies of so much of Banks's correspondence are available for reference. The editor and the Trustees of the British Museum are to be thanked for a production worthy both of the subject and of the institution.

W. B. TURRILL

AN INDIAN HISTORY OF SCIENCE

Bijnaner Itihas (A History of Science)

Vol. 2. By Sri Samarendranath Sen. In Bengali. Pp. xvi + 430 + 18 plates. (Calcutta: Indian Association for the Cultivation of Science, 1958.) Rs. 12.

THE first volume of this work (reviewed in *Nature*, 178, 1367; 1956) covered the period of ancient science up to the Roman empire; the second carries the story forward to the Renaissance and the birth of modern science. It amply fulfils the expectations aroused by its predecessor, indeed it surpasses them. The contents are divided into four parts. In the first part the author reviews the condition of scientific knowledge in medieval India. He discusses the contacts between Persia and the Mediterranean on one hand and China on the other, and carefully evaluates them. The most striking Indian contribution was in the field of mathematics and Mr. Sen summarizes the work of Varāhamihira, the sixth century polymath whom he calls the "Indian Pliny", of the great Āryabhat who—at the opening of the same century—calculated the correct value of π, of Brahmagupta, and of Bhāskara, the twelfth-century genius who explored the calculus. He further discusses the origins of the decimal system and the zero, and avoids the often exaggerated claims for their Indian antiquity. The Indian contributions, mainly by mathematicians, to astronomy are also worthy of remark, and Āryabhat even anticipated Copernicus. However, this field remained infertile largely because it was so much concerned with prognostication. Finally Indian contributions to medicine, chemistry, metallurgy and atomic theory are discussed.

The second part of the book deals with Arab science. Here too the material is presented in a sympathetic and balanced way. The great debt to Greek science is acknowledged as is the less-important Indian influence, and the achievements of al-Khwarizmi, al-Battani, al-Biruni and many others are outlined. A chapter is devoted to the Arab contributions to chemistry, particularly to Jabir, al-Razi and their followers; while in the field of medicine the name of ibn-Sina (Avicenna) stands forth.

With the third part of the book the scene is shifted to Europe and the background to the Renaissance. First, the survival of learning in the monasteries, the impact of the Carolingian renaissance, the effects of the Crusades and the influence of Arab science are considered; next the peculiar importance of the universities and their constitution are discussed. In this setting Christian and Greek learning mingle in Grosseteste and produce a Roger Bacon. The philosophy of Aquinas is outlined and leads up to a brief mention of the nominalists. It is indeed a joy to read in Bengali the translation of Occam's mighty razor. The section ends with a survey of knowledge in the thirteenth and fourteenth centuries.

The last part of the volume deals with the birth of modern science in the fifteenth century. First the author traces the technical discoveries which revolutionized life and thought: the magnifying glass, the clock, the compass, printing, and gunpowder. He then gives a full account of the work of Leonardo da Vinci. There follows a detailed history of the astronomical discoveries of Copernicus, Tycho Brahe, Kepler and Galileo. Next the great advances in anatomical knowledge are described, from Vesalius and Fabricius to Harvey. In chemistry, the work of Agricola is stressed and its practical importance is recognized. This second volume of the history of science ends with a short epitome of the seventeenth century as exemplified by Bacon, Descartes and Galileo.

It is indeed a pleasure to find in an Indian language so balanced and objective an account of this vast subject. This book carries with it something of the spirit which ennobles the writings of Sarton or Singer, and Mr. Sen is to be congratulated upon a remarkable achievement. As in the first volume the production is excellent, the illustrations are well chosen, numerous and well reproduced. It is impossible to overemphasize the importance of the history of science for education in India, and with the development of the regional languages the need for an adequate text-book is obvious. It is to be earnestly hoped that the Indian Academy for the Cultivation of Science may now take up the task of translating "Bijnaner Itihas" into the national language, Hindi, and the other regional languages, and that the Government of India may provide further support and encouragement for the task. We look forward to the publication of the third volume.

F. R. ALLCHIN

HUMAN DIVERSITY

Variation and Heredity

By Dr. H. Kalmus. (Survey of Human Biology.) Pp. xi+227+6 plates. (London: Routledge and Kegan Paul, Ltd., 1957.) 28s. net.

ASPECTS of human genetics, particularly the problem of assessing the changes in frequency of hereditary defects that may result from present or anticipated increases in the radioactivity of our environment, have been much in the public eye of recent years. Treatment in some sections of the Press, both in Britain and elsewhere, has often been emotional and invariably more imaginative than accurate. Even the controversies of the geneticists themselves have at times engendered more heat than light. Dr. H. Kalmus is therefore to be congratulated on the authorship of an objective and detached account of the factors, environmental as well as genetic, which contribute to human variability.

The book is the third volume of the "Survey of Human Biology" to appear. According to the publishers, the series is intended to serve three classes of reader, the inquiring layman, the student, and the specialist looking for information in fields other than his own. A clear and straightforward presentation is therefore required; also the avoidance of complexities and the limitation of technical jargon to a minimum. In these respects the author has succeeded admirably. Although the use of many technical terms is inescapable, the reader in return is entitled to have them clearly defined. Here Dr. Kalmus has been rather less successful. Definitions of a kind there are, but they by no means always appear at the first use of a term and the index is not always a reliable guide. This being so the usefulness of the book to its intended readers would have been increased considerably by the inclusion of a glossary. A comprehensive and up-to-date bibliography provides a partial compensation and is a valuable feature of the work.

The book is in no sense another elementary human genetics text, although genetics necessarily figures very prominently. The subject-matter is treated throughout from the point of view of its medical and social importance. Fourteen chapters of exposition are followed by three in which the wider implications for human affairs are discussed. The complex interaction of genetic and environmental factors is stressed and the absurdity of the supposed (by some) antithesis between 'genetically determined' and 'environmentally determined' characters is exposed. To those who have hitherto been unaware of this fallacy the reading of Dr. Kalmus's book should prove a salutary exercise.

There are a few minor errors and inconsistencies and one which may be more serious. On p. 139 it is stated that the genetic hazards of irradiation can be reduced by (among other methods) "... taking X-ray photographs instead of looking at the fluorescent screen, by which means irradiation with only two Röntgens can produce the same diagnosis as direct fluoroscopy requiring seventy-six Röntgens". Some readers are likely to take these figures to be gonad doses and since they have been told two pages previously that "... even such very low dosages as 0·3 to 0·1 Röntgen units per week or less ... constitute a potential threat to their [radiation workers'] progeny" they may well feel alarm. The actual dose which reaches the gonads will, of course, be greatly influenced by the part of the body under examination.

It is possible that doses of the magnitude mentioned may formerly have been delivered to the skin in some instances, but in contemporary practice (according to information given in a recent joint report of the International Committees on Radiological Protection and on Radiological Units and Measurement) gonad doses in even the most severe fluoroscopic examinations are likely to be at least an order of magnitude lower. This one slip apart, the book answers its purpose excellently and can be recommended to all who wish to have a readable and reliable statement of the present stage in the development of the study of human diversity. C. E. Ford

PHYSICAL AND CHEMICAL EXPLORATION OF THE CELL

General Cytochemical Methods, Vol. I

Edited by Prof. J. F. Danielli. Pp. xi + 471. (New York: Academic Press, Inc., 1958.) 12.80 dollars.

THE extraordinary growth in the number of 'annual reviews' or 'recent advances' series poses serious problems for contributors and editors. It is often very valuable for a research worker to review his own field, but once he has become established he may find himself the victim of an insidious process. It is flattering to be invited to contribute reviews and chapters and to take part in symposia; but there is a danger that many active minds are being diverted from research to writing. In some fields the number of reviews almost approaches the number of original papers. The relentless growth of such 'series' is partly to blame. Probably at no other time in the history of science have such a large proportion of reviews been written, and editors must be responsible for the careful selection of subjects and authors so as to avoid overlapping and repetition. The literature on cytological methods is already covered by reviews such as "Progress in Biophysics", "Advances in Medical Physics", and "International Reviews of Cytology," and collaborative works such as "Analytical Cytology", edited by Mellors, and "Physical Techniques in Biological Research", edited by Oster and Pollister.

It is a serious criticism of this new book that five of the nine subjects have already been dealt with (in some cases several times, and even by the same authors) in at least one of the publications mentioned above. Indeed the weight of cellular structures by X-rays (Engstrom and Lindstrom) and ultra-violet microspectrophotometry (Walker) have been the subjects of so many reviews that there is little new to offer. Both articles could have been held over for a year or two. The topics of Feulgen microspectrophotometry (Leuchtenberger), autoradiography (Pelc) and fluorescent antibody methods (Coons) have also been extensively reviewed elsewhere. It must be admitted that all these articles are well written and valuable in themselves, but it is rapidly becoming impossible for anyone to keep up with even the review literature.

The remaining four articles cover less familiar ground. Davies gives the fullest account (100 pages) of interference microscopy yet published. This is an admirable article and one wishes that every potential buyer of an interference microscope could be made to produce evidence that he has read and digested its contents. The exhaustive article (nearly 60 pages) by Bennett and Watts on the demonstration of sulphydryl groups by mercaptide coupling is perhaps less fortunate. One may admire the extraordinary thoroughness of the authors but it is surprising that the second longest article in the book was devoted to a method with (at present) such limited application. By contrast, the article by Holt on indigogenic staining methods for esterases is terse and severely practical. Finally, Danielli himself contributes a short article on the calcium phosphate precipitation method for alkaline phosphatase.

Having approached this book with a critical attitude, one wonders why, despite its imperfections, the general effect is a feeling of satisfaction. The answer is that not only is each of its articles authoritative and informative, but also the work as a whole preserves an integrity that is lacking in some other review journals. The articles are linked by a common theme and purpose and anyone concerned with cytochemistry can be certain that the majority of them will be of interest and value to him. Once this series is firmly established, it is to be hoped that reviews in this field will cease to be dispersed over a wide range of periodicals, thus making the task of the cytologist easier. Even though Prof. Danielli may not have got off to a perfect start, one feels that he is likely to make a very strong finish. R. Barer

PALÆOPEDOLOGY

Soils for the Archæologist

By Dr. I. W. Cornwall. Pp. 230. (London: Phoenix House, Ltd., 1958.) 50s. net.

MANY pedologists, like the reviewer, have no doubt been consulted from time to time by archæologists about problems that have arisen in the course of their excavations. That adequate help has not always been forthcoming is in the main due to lack of understanding between the two disciplines, and it is Dr. I. W. Cornwall's aim to reduce this to a minimum. The book is primarily directed at his archæological colleagues, but pedologists could read with advantage Part I of the book and the last chapter, both of which are devoted to a discussion of archæological deposits, but also containing useful information on loess, cave earths and peat. The core of the book is an account of soil types and some methods for their examination, and it is here that the pedologist will find most to argue about. The systematic discussion of the soils is based on Kubiena's "The Soils of Europe", with little modification. While from the morphological point of view this is, in the main, satisfactory, the theories of the underlying processes contain much that is pure guesswork and very debatable. Although Kubiena's techniques are now widely used, his classification is not generally accepted and it would have been helpful to have mentioned soil groups recognized by other workers, even though an accepted synonymy is not yet established. This would show that what is commonly called a podzol or podzolic soil in the U.S.S.R. need by no means correspond to Kubiena's definition although it might fit one of his other groups. In this connexion a set of photomicrographs of the types of fabric should have been provided.

There is much use of the theory of peptization of iron oxide by silica for which there is no good evidence, although silica sol will peptize clays. In the British Isles (cf. p. 98), as elsewhere in the temperate zone, water-soluble silica can be extracted from soils, and is therefore presumably hydrated. The remarks about the colour changes of hydrous iron oxides on dehydration are open to question, for it is a fact that in many red soils goethite is the main identifiable form. Crystal growth is a more probable explanation of the colour changes. The iron oxides in a braunerde are said to be flocculated, and therefore immobile, so that concretions do not form (Kubiena, p. 234), but Dr. Cornwall allows them to be "typically seen in braunerde" among others. This may be true if one uses the more general expression 'brown earths'. Such concretions formed in the earlier history of the soil do not necessarily shrink and become deformed (p. 191) but may retain their shape and structure. Again, a braunerde does not necessarily become degraded to a podzol on increase in acidity; unless heath intervenes, a form of sol lessivé is a more likely result.

The author's descriptions of laboratory techniques are unorthodox but in general probably adequate. In mechanical analysis, however, it is better to use 'Calgon' systematically unless the coarser fractions are examined for aggregates of silt and clay. The removal of gypsum is readily effected by ammonium acetate. In the method for the determination of *p*H (p. 166) the proportion of soil to water is surely a misprint. Under iron, mention might have been made of a method for 'free' iron oxide, the determination of which is commonly more useful than total iron. It should also be pointed out that a sharp increase in total iron in the subsoil does not necessarily indicate podzolization, for this effect is shown by grey-brown podzolic soils (sols lessivés). The observed variation in *p*H with depth in this group of soils (also in some tropical soils), namely, a minimum value in the lower *B* horizon, suggests an alternative explanation of the results of the Mersea section (p. 207). The top of the decalcified layer could well be the surface of the buried layer rather than the point of minimum *p*H as seems to be assumed by Dr. Cornwall.

A pioneer effort like this book must inevitably have its defects, but the author has made a valiant attempt to provide a bridge between two disciplines that should lead to valuable results in the future. Alex Muir

SEMI-CONDUCTORS

Solid State Physical Electronics

By Prof. Aldert van der Ziel. Pp. x+604. (London: Macmillan and Co., Ltd., 1958.) 37*s*. 6*d*. net.

The expanding use of semi-conductor and dielectric devices during the past decade or so has been so rapid and widespread that there now exists in the design and applications of these devices what is virtually a new branch of electrical engineering. The development of these devices has been accompanied by the publication of a number of books written primarily to provide accounts either of the special circuit techniques involved in their use or of the relevant aspects of solid state physics. However, this book provides a new approach by aiming at giving an understanding of the *operation* of solid state devices. The book attempts to cover this whole field in a single volume designed to fill the need for a collected and concise account of the exploitation of the physics of the solid state over the whole of this rapidly expanding subject.

The first five chapters of the book deal briefly with the relevant basic physics required. Topics which are discussed include particle and wave aspects of light and matter, particle statistics, and the structure and band theory of solids. The next six chapters form a section dealing with the various mechanisms of electron emission from solids, and the design and characteristics of relevant devices such as thermionic vacuum tubes, photo-tubes, and secondary emission multipliers; approximately half this section is devoted to thermionic emission and its applications. The physical principles and operation of the more important semi-conductor devices are treated in the next six chapters. Metal to semi-conductor rectifiers and photo-effects in semi-conductors occupy one chapter each, but most of this section is concerned with a relatively extensive treatment of the junction diode and in particular the transistor and its equivalent circuits. Dielectric and magnetic materials and their applications are dealt with in the remaining six chapters. Topics discussed here include luminescence and the light amplifier, transducers, ferroelectricity and the dielectric amplifier, the solid state maser, and ferrite devices.

It is inevitable that, in covering so wide a subject in a single volume, some applications have to be omitted; for example, no mention is made of parametric amplification. The discussion of topics included is necessarily curtailed although each chapter is followed by a short list of references to original literature and additional texts for supplementary reading. Formulæ required are sometimes quoted without derivation, for example the equations for Fermi-levels in semi-conductors given on p. 90; and physical concepts are sometimes introduced without discussion of their background, for example the introduction of thermodynamic free energy on p. 511. However, since the emphasis of the book throughout is on providing an understanding of the operation of devices rather than on giving a detailed exposition of fundamental solid state physics or circuit engineering, this is not necessarily a disadvantage.

The book is well written and printed, and is easy to read although the large number of extensive footnotes employed does tend to break up the reading of the text. Unfortunately, the value of the book is reduced slightly by the presence in it of a number of minor errors such as observations in the text which disagree with the relevant diagram, for example the Fermi-level in Fig. 12.3*b* is raised and not lowered; numerical magnitudes given wrongly, for example the spontaneous polarization of barium titanate given on p. 526 should be about 0·26 C.m.^{2}; and misprints in the text such as the Fermi function on p. 51 and the thermoelectric power quoted for metals on p. 463. Most of these are trivial but do cause some confusion and irritation.

As is the growing practice in this field, the book utilizes the M.K.S. system of units, includes a useful short table of fundamental physical constants, and gives a number of representative problems, with answers, at the end of each chapter.

To the student of engineering or physics, this book provides a useful and comprehensive introduction to the many different ways in which solid state physics is at present being exploited; to the specialist worker in this field the book will serve as a reminder of the very wide ramifications and potentialities of his subject. Notwithstanding the various criticisms made here of this book, there is no doubt it is an important publication and can be recommended widely.

G. T. Wright

SURMISE AND FACT ON THE NATURE OF CANCER

By Dr. PEYTON ROUS, For.Mem.R.S.
Rockefeller Institute for Medical Research, New York

THE hypothesis according to which tumours are due to mutations of somatic cells was first brought forward by Boveri in 1902 and has been debated ever since. It was presented anew last July at one of the few plenary sessions of the International Cancer Congress in London. The state of mind of many research workers when this Congress ended has been reported as follows[1]: "Some hoped that cancer can be eradicated without an understanding of its very nature; others felt that we must understand better the enigma of the cancer cell and even of life itself. If the somatic mutation theory of cancer is right, then development of cancer is an inherent property of life, and cancer research is but in its lusty infancy".

Obviously a great deal depends on whether the hypothesis is right. For what men think determines not only what they do but also what they do not; and numerous workers on cancer are now content to think that it results from somatic mutations. Hence they see no reason to seek in other directions to learn its nature. The factual basis for this state of affairs will be considered here, as also the share of the hypothesis in the advancement of knowledge. Important reasons exist for doing this—the biological importance of the cancer problem, its urgency for man, and the present state of mind of many scientists now investigating it, as just mentioned.

During the first years after Boveri proposed the mutation hypothesis[2] the changes of normal cells resulting in tumour cells were held to occur "of themselves", like germinal mutations: and since the changes appeared to be abrupt and discontinuous, as in the case of these latter, and also heritable, being passed on at every cell-division, the assumption seemed warranted that they might be due to genuine mutations—but of somatic cells dying with the organism. Now we know that neoplastic changes are not spontaneous, but are induced by extraneous agents or conditions, in the generality of instances, and almost certainly in them all. It has become rule of thumb, on finding a tumour, to look for the agent bringing it on. Hundreds of agents which do this—the so-called carcinogens—are now known, and new ones are continually being discovered. Most of them act slowly, some effecting neoplastic change only after many years; but their influence is cumulative, no matter how long the interval between exposures to them, and eventually they render some cells neoplastic. They are of the most heterogeneous character, ranging all the way from radiant energy and highly various substances, to viruses and animal and vegetable parasites. Yet, except for the viruses, they have little determining influence on the character of the growths they induce. In doing so they play upon the neoplastic potentialities a tissue possesses, and these differ not only with the kind of cell implicated, and the species of animal, but even with its breed. Some carcinogens reach deep into the body, and others are made there.

This new knowledge has large practical bearings as witness the demonstrated relationship between cigarette smoking and lung cancer. As yet, however, it has thrown no piercing light on the nature of neoplastic change. The great majority of the carcinogens are merely provocative: they convert normal cells into tumour cells but have no further essential role and are degraded or left behind as the changed cells multiply. Their relation to the neoplastic state may be likened to that of ignition to combustion: a fire can be kindled in any one of numerous ways but, with this done, its decisive share in events is ended. The analogy can be pushed further: flames differ according to their ingredients and tumours differ according to the type of cell involved.

The realization that tumours are induced phenomena made necessary an adjustment of the mutation hypothesis. According to present thought, the carcinogens induce mutational changes and these result in the growths—upon which they may have some selective effect, a corollary presumption. In this form the hypothesis becomes most attractive, providing as it does a blanket explanation for almost the whole diverse world of the neoplasms. Yet not for quite all of them. How does it account for the small but gradually enlarging group of tumours that are produced by viruses, which, incidentally, determine their character, and are made up of cells in which these viruses multiply and from which they can be recovered in a condition to produce more tumours of the same sort? A first inclination was to exclude the growths from consideration as not genuine neoplasms: and this has recently been attempted anew, despite proof that they measure up in all ways to the classical definition of what tumours are, save in that their cause has been found. To reconcile their existence with the mutation hypothesis some workers now consider the causative viruses to be 'transmissible mutagens' affecting the genes of somatic cells.

Needless to say, somatic mutations, recognized as such by the geneticists, do occur. They are frequent in plants and now and again are found in the lower animals but are exceedingly rare in the higher. They are regularly cited by such investigators as hold that tumours are due to somatic mutations, and with reason, since without them this assumption would have no directly factual basis. The earlier they occur in the development of an organism the greater is their share in it, through multiplication of the affected cells. Occasionally one of them finds expression in the vertical half of a plant, not infrequently in a branch or leaf or flower, and often in the mere segment of a petal, when that petal had already begun to form before the mutation occurred. The changed branch or leaf or segment still retains the form and functions of such, but differs from the normal in colour or texture or both. But it is significant that none of the plant tumours thus far studied has been found in association with these mutations.

In the higher animals somatic mutations are so seldom come upon as to gain individual report. They have been noted very occasionally in pigeons, guinea pigs, sheep, rabbits, and rats. Half the body of a pigeon may be covered with black feathers instead of the normal grey of the opposite half; or a patch of skin on a guinea pig or rabbit may carry fur having a colour different from that to be expected by its inheritance; or a patch of wool on a sheep may be notably shallow as compared with its fleece elsewhere. These anomalies are not passed on to the next generation. The cutaneous patches have been aptly termed 'mosaics'; for they are surface phenomena, the skin with the abnormal fur or fleece remaining level, and its cells retaining their normal place and activities, not extending downward or laterally at the expense of the adjacent tissues, much less proliferating into a mass as tumour cells do. Few, if any, somatic mutations seem ever to have been observed in mice, which is the more surprising because, throughout many years, thousands of these animals have been under close scrutiny in the Jackson Laboratory at Bar Harbor, Maine, a laboratory largely given over to the experimental study of mouse genetics, much of it by inbreeding. This latter has resulted in numerous homogeneous strains of mice useful for scientific purposes, some prone to develop tumours of one organ or another in a high percentage of instances; yet no breed has yet been reported having any discernible tendency to somatic mutations of recognized type. Only plant instances find mention in the numerous papers from the Jackson Laboratory, wherein the somatic mutation hypothesis has been advocated.

Still more remarkable is the fact that no valid 'mosaics' have been reported for human skin, so accessible as this is to constant inspection and so intimately inspected. It may well be that they occur; but if so they have been ascribed to some cause other than somatic mutations. The only phenomenon indicative of them in man is the occurrence of paired eyes of markedly different colour, one blue and one brown, for example, when they should resemble each other by inheritance. The deeper human organs have been searched microscopically for more than a century, yet no abnormalities have been reported by pathologists that can be referred with any assurance to somatic mutations.

In 1932, J. S. Haldane[3], after studying the somatic mutations then available, wrote that "the known alterations in [cell] character which can be referred to chromosomal changes are of a much less fundamental kind than would be required to explain malignancy in tumours. . . . Even when a chromosomal mutation is inconsistent with the ultimate survival of the developing organism [its] growth is still co-ordinated". This latter fact is well exemplified in the ill-matched eyes already mentioned, as also in 'sheep mosaics', which, alone among those of animals, have been examined with the microscope. This has shown that the skin involved in the mosaics has the normal aspect, except that its hair follicles are smaller than usual and form smaller hairs. The cutaneous cells give no sign of increased ability to proliferate, much less to do so independently of the organism. Here lies the crucial difference between neoplastic cells and those that have undergone somatic mutations of the kinds thus far recognized.

One can readily understand why somatic cells that have undergone authentic mutations such as those thus far reported should rarely manifest themselves. Their lack of any increased ability to proliferate must result in their virtual imprisonment within the normal tissue context, unless indeed they have mutated early in the development of the organism to which they belong. Actually, in the adult creature, many tumour cells are unable to assert themselves even when possessed of considerable ability to grow. But if they are provided with space, as by cutting away the tissue next to them, or if the tissue in which they lie is stimulated chemically, such hidden cells may promptly form tumours[4], their proliferation far exceeding that of the adjacent, and competing, normal cells of the sort from which they have derived. Not so with cells that have undergone authentic somatic mutations of the kind above described: their growth fails to exceed that of their normal fellows. Only when they have mutated so early in the life of the embryo as to share to a recognizable extent in its formation can they be expected to multiply sufficiently to gain attention.

If one could only bring chemical carcinogens to bear on mammalian embryos at an early stage, one might learn whether these agents are mutagenic as well; but nearly all of them fail to get through the placenta. Radiant energy does reach into the uterus, and malformations due to its action on embryos have been described, but no somatic mutations. Fortunately, one chemical carcinogen, ethyl carbamate (urethane), which induces lung tumours in mice, and is frequently mentioned by the somatic mutationists because it causes germinal mutations in *Drosophila*, does pass the placental barrier[5]; and it acts with such swiftness on the embryos of mice of some breeds, when these are injected with it while pregnant, that adenomatous tumours can be perceived in their pulmonary tissue within three days after birth[6]. The lungs are almost as well suited as skin to the disclosure of somatic mutations, because the least morphological change in their delicate, orderly, alveolar web can be discerned: yet even when urethane is brought to bear on the embryos almost as soon as their pulmonary tissue first begins to form, and daily thereafter, through injection into their mothers, no signs of somatic mutations have been found in serial sections of their lungs, obtained at intervals from their birth to maturity, but only the well-known adenomas—growths capable of forming a succession of tumours when serially transplanted.

On turning now to the tumours themselves that are ascribed to somatic mutations, one learns much that is pertinent. The assumption is often tacitly made that the changes in aspect and behaviour which occur when normal cells become tumour cells are consequent merely on their increased proliferation. But only exceptionally, and in cells of a few sorts, do neoplastic changes seem to result only in an increased capacity to grow. In such cases the increase is slight (for example, some fatty tumours of man, certain liver tumours of mice). Of course, when neoplastic cells multiply rapidly they have less time to differentiate and hence tend to diverge more from the normal; but those of many cancers exhibit great distortions of form and function, irrespective of whether their proliferation be fast or slow. The cells of such tumours are almost grotesque in aspect and worse in behaviour, invading, destroying, scattering to other organs, and multiplying so rapidly that they outstrip the ability of the body to supply them with blood vessels and in consequence die in hordes. Cancerous cells much less changed than these still differ strikingly from normal cells. One is reminded again of Haldane's dictum that "the known alterations in [cell] character which can be referred to chromosomal changes are of a much less fundamental kind than would be required to explain malignancy in tumours".

The cells of the most fatal human cancers are far removed from the normal in character, and almost no growths fill the gap between, much less a graded series of them, such as one might expect were they the outcome of random somatic mutations, all tumours in this series, or rank, consisting of neoplastic cells of the same derivation but diverging more and more from the norm in the direction of the malignant state. Cancers of the human lung are exceedingly common whereas pulmonary tumours of any other sort are rare; gastric cancers outnumber more than 20 to 1 the benign adenomas derived from cells of the same sort; and cancers of the epithelium lining the body of the uterus and its cervix are frequent, whereas adenomas are uncommon. In none of these instances can the rarity of the benign tumours be ascribed to any lack of free space in which they may assert themselves, nor are stimulating influences wanting to them. Furthermore the benign tumours are in a much 'healthier' state than the malignant, and hence their scarcity cannot be ascribed to any inability of their cells to survive. Wide differences, crucial to the patient, separate growths of the two kinds. To all practical intents and purposes the cancers are discontinuous, episodic phenomena; yet they are so repetitive that the clinical pathologist can predict the course of this one or that out of his past experience with others of the same sort.

The absence of any ordered gradation of tumours, their discontinuous incidence, can be seen in animals as well. By inbreeding litter mates throughout many generations, strains of mice have been obtained which carry a liability to tumours of one sort or another, as already mentioned. Those of some breeds have mammary growths, others lung tumours or liver tumours or bone tumours, and yet others leukæmia. The growths of the mamma and lung have been most closely studied. In the lung they are always benign adenomas of distinctive morphology, whereas in the breast they are equally characteristic, epithelial cancers. Though they are episodic phenomena, several often arise in a single animal.

Nearly all ageing female mice of some breeds die of mammary tumours, and though less frequent in mongrel mice they are the most common of all growths. Hence they were the main material studied during the first ten years of experimental cancer research. They could only be propagated by transplanting their living cells, and the failure of all efforts to extract a causative agent from them led to the conclusion fifty years ago that they were consequent on innate, cellular changes. They became indeed the very citadel of the belief (revived anew during the recent International Cancer Congress) that the riddle of cancer will be solved only with that of life itself; and, like the other tumours occurring 'spontaneously' in genetically homogeneous mice, they were long held to be due to an inherited tendency. So matters stood until 1934 when a Dutch worker and a group at the Bar Harbor Laboratory discovered independently that this tendency is passed on through the mother. A little later, one of the Bar Harbor group demonstrated that their cause is a virus passed to the young in their mother's milk, yet causing no harm until after they mature, when cancers develop in consequence of its action. Do viruses account for the other tumours occurring in inbred mice? The organs of all are identical in form and function; yet growths of this sort or that arise in this or that breed, whereas not in others. What can be the *tertium quid*? The fact that a carcinogen, 20-methylcholanthrene, hastens the occurrence and increases the frequency of the cancers determined by the milk virus, and also that of the lung adenomas and leukæmias already mentioned, possesses a suggestive significance in this connexion. Indeed, recently a leukæmia of the mouse has yielded a virus that quickly produces the disease in others[7].

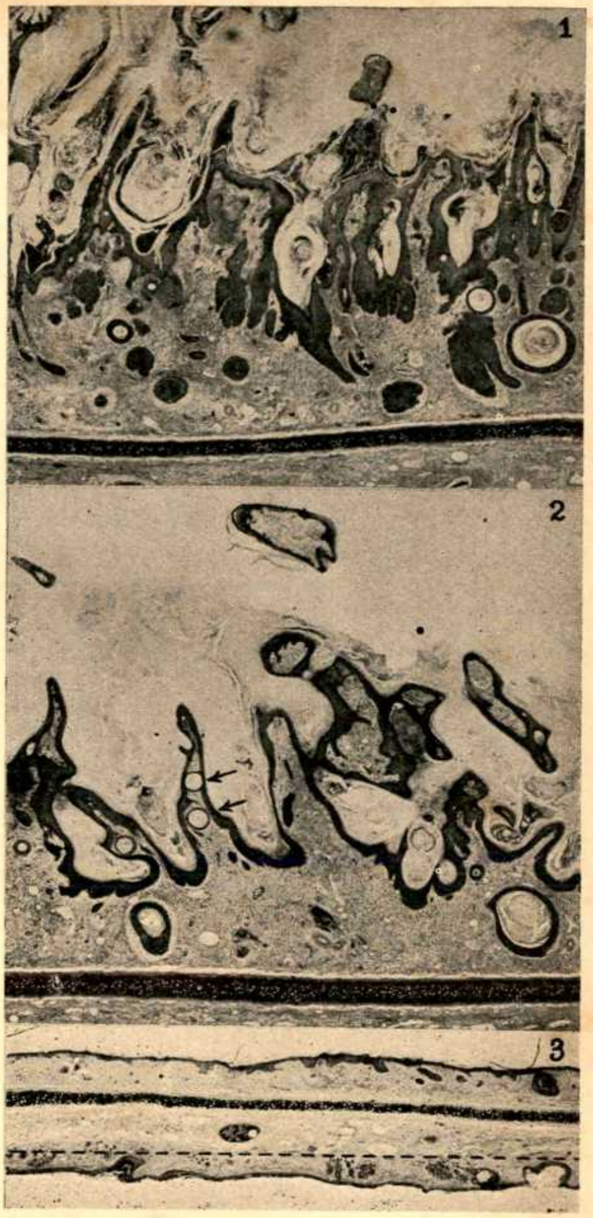
Many experiments have been made of late to learn whether carcinogenic agents cause somatic mutations in the lower forms of life[8]; and the advantage of using micro-organisms has been pointed out, these undergoing no separation into somatic and germ cells. Tests of them, as also of *Drosophila*, have shown beyond doubt that some carcinogens can induce permanent biochemical changes in cells exposed to them. Two distinguished investigators[9] sum up the results of their recent work on the mutagenic effects of carcinogenic hydrocarbons upon *Neurospora*, and "other similar findings", with the statement that they are "at least not inconsistent with the somatic mutation hypothesis". The evidence as a whole makes plain though that some carcinogens induce somatic mutations whereas others do not, that some mutagenic agents fail to be carcinogenic, and that many substances closely related chemically to agents of both sorts do neither[10]. Persistent search has been made, ever since Boveri's time, for chromosomal alterations which might prove characteristic of the neoplastic state—all to no purpose.

Cancer cells often undergo further discontinuous changes, and these have been many times noted in cultures of the normal, somatic cells of mammals; but since normal cells can proliferate endlessly *in vitro* the only way to tell whether they have become neoplastic is to return them to creatures of the kind from which they derived. This has been done, and mouse fibroblasts long exposed in culture to methylcholanthrene have given rise to sarcomas. But the control cultures became sarcomatous also. This would be astonishing were it not known that some substances deemed innocuous, lard, for example, will induce sarcomas after injection amid the fibroblasts of intact mice or rats. The cultures maintained longest, and yielding most sarcomas, though of late with no carcinogen purposely added, had been grown for several years on sheets of 'Cellophane', a material recently shown to induce sarcomatous changes when embedded amid the connective tissue of rats and mice[11]. Other foreign materials that might be carcinogenic have been present in the fluids nourishing the cultures—horse serum, extracts of chick or bovine embryos, and human amniotic fluid or serum from the blood of the umbilical cord. In one set of exquisite experiments, fibroblasts from the heart of a rat were cultivated in a mixture of cord serum and chick embryo extract, and throughout 2½ years the air about them was repeatedly replaced by nitrogen for the maximal period that the cells would survive. On return to rats at the end of this time the cells gave rise to sarcomas whereas those of the control cultures, maintained without anaerobiosis, did not[12]. One is reminded of the sarcomas arising now and again in human arms which have for years been poorly oxygenated because greatly swollen as a result of operative interference with lymph drainage[13]. It would appear that carcinogenic conditions—conditions that is to say which bring on the neoplastic state—have determined both the human tumours and the malignant changes occurring in cultured rat fibroblasts.

The term 'mutations', instead of the objective term 'variants', is often applied nowadays to the discontinuous changes occurring in somatic cells grown in tissue cultures. But how many of them deserve the name ? The neoplastic viruses bring about wholly analogous changes in the cells of intact animals, and they would surely be ascribed to somatic mutations by the advocates of this hypothesis had not their causes been found. One is reminded in this relation of the numerous 'orphan' viruses that have turned up of late in tissue cultures, strays from unknown sources, as also of the fact that Newcastle virus can persist in tissue cultures without giving any cellular sign of itself, yet be roused to pathogenicity by experimental procedures[14]. Scientists have only begun to realize that microbiological entities, distinct from the apparatus of cells, may accompany these, and do no one yet knows what. The discovery of a 'Kappa factor' in the cytoplasm of *Paramecia* provides an instance in point. One should not presume on this realization, but it cannot be dismissed. While adventuring into the infinitely great we are experiencing what the exceedingly small can do to us.

When Boveri first outlined his idea that tumours are consequent on somatic mutations[2] he pointed out that it was not incompatible with the assumption that their primary cause is parasitic in nature. Indeed, he inclined to this possibility, having noted that physical and chemical insults can cause multipolar mitoses to occur in sea urchin embryos. In this connexion an extraordinary, recent revelation should now be mentioned, namely, that bacterial viruses sometimes transfer genetic material from one kind of bacterium to another, the result being an enduring transformation of the latter[15]. Several workers have suggested that the neoplastic viruses do something similar to the normal cells of animal tissues, inducing somatic mutations that convert them into tumour cells. The question might be asked whether this reconciling assumption (of transmissible mutagens) may not apply to viruses producing growths which fall somewhat short of the standard for typical neoplasms—to the Shope fibroma virus, for example, which causes rabbit growths that resemble tumours in all important ways except that after some weeks they regress : and if to the Shope fibroma virus, surely to the virus of rabbit myxomatosis into which it can be readily transformed. Myxomatosis is a fatal inflammatory process, though entailing some cell proliferation ; and certain strains of vaccinia also cause cells to multiply though they die soon after. Now one comes to the frankly necrotizing viruses. What of them ? Is one to suppose that they kill cells rapidly by transferring genetic material to nuclei, or are they directly lethal ?

These justified questions carry no implication that viruses are harmless to the genetic apparatus of cells. They may well play havoc with it. But to assume this in the case of neoplastic cells is less than neces-



Figs. 1–3. Effects of scharlach *R* in olive oil when placed beneath rabbit epidermis. A tourniquet was applied to the ear of an anæsthetized rabbit, stopping all circulation to its distal third, and then olive oil saturated with scharlach *R* was injected into a marginal vein of this third, under such pressure as to rupture many capillaries. As a result, numerous tiny droplets of oil escaped into the subepidermal tissue

Fig. 1. Inner side of an ear 23 days after injection. The epithelium has undergone an enormous proliferation and has extended down toward the oil droplets. Both in aspect and behaviour it appears cancerous

Fig. 2. Later stage, with the dye almost gone from the oil. Epithelial invasion has ceased, and many of the droplets are surrounded by a layer of what now looks like ordinary epidermis, and are in process of extrusion (arrows)

Fig. 3. Ear 69 days after injection. It has nearly returned to the normal. Numerous lacunæ where oil still persists can be seen on the outer (under) side of the ear ; but on its inner side, where the tissue was tightly bound to the cartilage, few are left

The portion of the ear shown in Figs. 1 and 2 lies above the broken transverse line in Fig. 3

(Eosin and methylene blue stains : all are at the same magnification) sary. In 1906, a German pathologist, seeking some substance that might be the cause of cancers, found that a dye, scharlach *R*, when dissolved in olive oil and injected beneath rabbit epidermis, would cause its cells to behave as if malignant[16]. This finding was soon confirmed by numerous workers: to all appearance an actively invasive, squamous-cell carcinoma is called forth by the dye (Figs. 1–3). But not for long: the epidermal cells revert to the normal as its influence wears off.

Here is no somatic mutation. The physical character and chemical activities of the neoplastic viruses, as such, may well be the cause for the neoplastic changes they produce, changes passed on from one cell to another because the viruses themselves multiply and are passed on.

At the time of writing, the somatic mutation hypothesis, after more than half a century, remains an analogy: "it is presumptive reasoning based on the assumption that if things have similar attributes they will have other similar attributes"[17]. No discoveries that tighten this analogy have been made. Of course, one can assume that tumours are due to somatic mutations of some qualitative type unrecognized as yet, thus piling surmise on surmise.

A hypothesis is best known by its fruits. What have been those of the somatic mutation hypothesis? It has resulted in no good thing as concerns the cancer problem, but in much that is bad. It has led within the year to an authoritative statement, in the lay Press, that since cancer is certainly due to somatic mutations, the possibility of having it is "inherent"; and that this being so, the most man can ever do is to palliate such malignant tumours as may have become disseminated in the body and to avoid new carcinogens as well as the old.

Here is fatalism to blast many a hope and effort. Fortunately, the public, now empowering large-scale attempts to cure cancer, are a hard-headed generation. They have learned the lesson of the antibiotics, substances that do deeds transcending all medical preconceptions.

Most serious of all the results of the somatic mutation hypothesis has been its effect on research workers. It acts as a tranquillizer on those who believe in it, and this at a time when every worker should feel goaded now and again by his ignorance of what cancer is.

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THE CHAPELCROSS NUCLEAR POWER STATION

By J. C. C. STEWART

THE Chapelcross Works of the United Kingdom Atomic Energy Authority, which was opened on May 2, is situated about two miles to the east of Annan, Dumfriesshire, Scotland.

The Works consists of four gas-cooled graphite-moderated reactors, each of 180 MW. heat design output with electricity generating plant of 140 MW. electrical net design output, together with the associated ancillary equipment. The output will comprise irradiated uranium containing plutonium of military grade with electricity as a by-product.

Construction started at Chapelcross in 1955, and the first reactor was commissioned in February 1959. The existing programme calls for the station to be fully commissioned in March 1960.

Early in 1955 the decision was taken to increase the production of plutonium for military purposes. At the time the construction of Calder Hall was well under way. Investigation showed that the Calder site could only be doubled in size to give a four-reactor station. The increased production demands required a six-reactor programme over and above the two original Calder reactors. Accordingly, a site suitable for a four-reactor power station was sought in reasonable proximity to the Windscale plutonium factory to ease the transport problem associated with the irradiated material. The Chapelcross site, a former Royal Air Force airfield, was chosen in May 1955. Fuel supplies for the reactors come from the Springfield Works of the United Kingdom Atomic Energy Authority in Lancashire.

The major items of the Station are identical with those at the Calder Hall Works, the details and performance of which have been described elsewhere[1,2], but modifications based on experience at Calder Hall have been introduced where appropriate. There are, however, large differences in overall layout. As the Chapelcross construction plan called for a four-reactor station *ab initio*, the reactors were conveniently built in line, this arrangement allowing the use of a single large turbine house with four adjacent cooling towers. Geographical compactness is thus achieved compared with the protracted *A* and *B* station layout on Calder, a factor which should ease operating and maintenance problems. As the station is about 75 miles distant from the plutonium factory at Windscale, it has been necessary to provide a water-filled storage pond for irradiated uranium to provide flexibility in operation and to ease the transport problem.

A recent modification of design introduced on Chapelcross reactors Nos. 2, 3 and 4 concerns the introduction of removable graphite sleeves into all fuel channels, to provide a solution to the problems

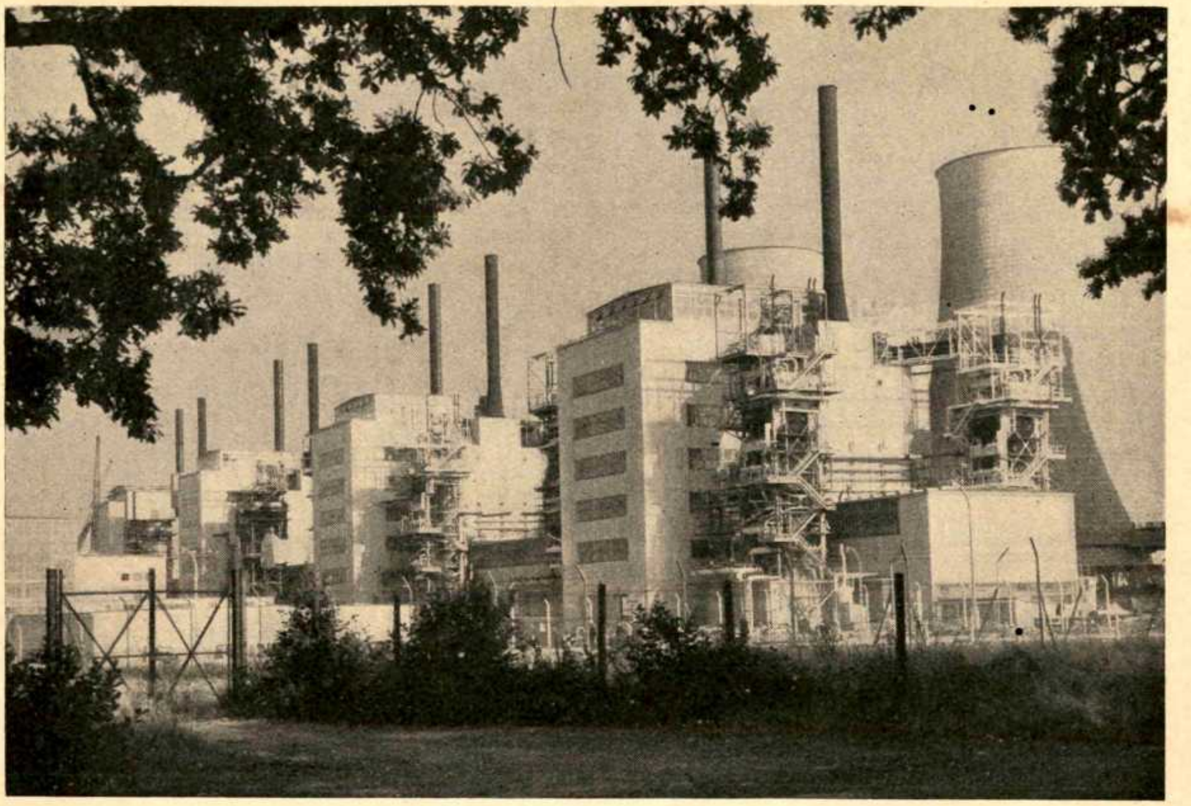

Fig. 1. Chapelcross Nuclear Power Station. Copyright reserved: U.K. Atomic Energy Authority, Risley

of stored energy associated with irradiation damage of the graphite moderator.

The results of this damage are usually described as Wigner effects after E. Wigner, who, in 1942, predicted that atoms in moderators would be displaced by fast neutrons. Those displacements could be permanent in the absence of annealing, with corresponding changes in physical properties. The present model assumes that a moving carbon atom which has suffered fast-neutron impact at first loses energy principally by electronic excitation. As its energy diminishes there is an increasing probability of an elastic collision with other carbon atoms and this creates a group of displaced carbon atoms situated at interstitial sites together with a corresponding set of vacant lattice sites. The physical results of these displacements appear as changes in thermal and electrical conductivity, elastic constants, thermal expansion, Hall effect, physical dimensions and heat of combustion. It is the two latter properties which largely affect reactor design and operation.

Changes in physical dimensions are catered for by utilizing the differing growth-rates along the various axes, by permitting adequate growth clearance where necessary and by allowing unrestrained growth in directions not associated with critical alignments.

Changes due to heat of combustion are due to the stored energy, inherent in the carbon atom displacement process, which may build up as irradiation proceeds.

In the event of graphite with a stored-energy content being heated sufficiently above the normal temperature at which irradiation occurs, release of the stored energy will be initiated. Moreover, after sufficiently long irradiation, it is possible to have a stored-energy content per unit mass greater than the specific heat of the graphite. With the appropriate combination of the above circumstances, a stored-energy release could be self-propagating and could lead to high graphite temperatures with consequent hazard to reactor operation.

Fortunately, the changes in physical properties are decreased as the irradiation temperature is raised, due to the increased mobility of the interstitial atoms, with increased probability of self-annealing. This factor has eased considerably the stored-energy problem at Chapelcross and Calder compared with the Windscale reactor, the respective gas inlet temperatures being 140° C. and 20° C. However, no further raising of inlet gas temperatures is possible with the existing reactors by virtue of temperature limits on the blow casings and inlet ducts. Accordingly, an alternative solution has been found in the provision of removable graphite sleeves in the channels, which are so designed that a small gap is left between them and the bulk of the graphite. This gap acts as a thermal barrier between the moderator and the coolant, and ensures that the temperature of the bulk graphite is raised above its normal value.

This solution has two variants in that different methods are possible for reactors which have operated and for reactors which are under construction. In the second case, it is possible to modify the core bricks prior to erection and to fit removable graphite sleeves without reducing channel diameters. This solution is being adopted for Chapelcross reactors Nos. 2, 3 and 4. No. 1 reactor will use the alternative method of sleeving, whereby 'Magnox' sleeves are lowered into unmodified channels, if this is necessary in the future. This latter operation reduces reactivity and channel flows, thus reducing power, and adds appreciably to the times during which a reactor is out of action. Hence the graphite sleeve solution has been adopted wherever possible.

The water-filled storage pond for irradiated uranium is a feature not provided at Calder Hall owing to its close proximity to the Windscale ponds. The addition of the pond makes Chapelcross more akin to the new nuclear power stations now under construction for the Central Electricity Generating Board and South of Scotland Electricity Board, these also having individual storage ponds. The pond at Chapelcross has sufficient capacity to hold a number of cartridges equivalent to about three reactor charges. Irradiated fuel will be taken to the pond using standard containers holding twenty-four cartridges, will be left to decay for some months and will then be transported by road to the plutonium-processing plant at Windscale.

The major functions of the pond are to ensure that transport delays do not affect the times during which a reactor is out of action, and to ease the transport problem so far as vehicles, containers and man-power are concerned.

The Chapelcross reactors, like those at Calder, can only be refuelled when they are shut down and when the coolant gas pressure is at near atmospheric. It has been found that the refuelling time virtually determines the time the reactor is out of action, any necessary maintenance can be effected simultaneously, and hence it is essential to keep refuelling time to a minimum to ensure maximum production. The pond assists in this by providing a storage point in the fuel cycle and thus allowing refuelling operations to be almost entirely independent of external transport arrangements.

The second advantage of the storage pond is that it permits utilization of the natural radioactive decay of the irradiated fuel elements. Any decay eases the shielding problems associated with any subsequent handling operations. After the delay period, it is estimated that it will be possible to transport from Chapelcross to Windscale six times as many cartridges per container as is possible for Calder to Windscale. The Chapelcross containers are about 50 per cent heavier, but there is nevertheless a gain factor of four in the number of cartridges per container, thus diminishing the requirement for containers, vehicles and man-power.

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OBITUARIES

Sir Robert Muir, F.R.S.

Sir Robert Muir, emeritus professor of pathology in the University of Glasgow, died in his ninety-fifth year on March 30 at Edinburgh, where he had lived in retirement for some time. He was born at Balfron, Stirlingshire, on July 5, 1864, but soon afterwards his father, a clergyman, was called to Hawick, and he grew up there. He graduated in arts at Edinburgh in 1884, M.B., C.M. with first-class honours in 1888, and M.D. with honours and a gold medal in 1890. He entered the Pathology Department under Greenfield with a Vans Dunlop Scholarship, and there began his original investigations into the reactions of the leukocytes.

Muir's scientific contributions fell into four main divisions. First (1888–1902) there were his studies on leukocytosis, which established that the enormous increase in the number of neutrophil polymorphonuclear leukocytes found in certain infections resulted from proliferation and differentiation of the finely granular myelocytes of the bone marrow; the significance of the leukoblastic reaction was thus revealed. Secondly, studies on immunity (1903–12) were concerned chiefly with the properties of hæmolytic antisera. Results obtained by rigorous quantitative methods led to a brilliant analysis of the antibody–complement mechanism. *Inter alia,* it was shown that, whereas complement is firmly combined with the antigen, the immune-body remains dissociable. This is incompatible with a supposed 'amboceptor' constitution of the latter. The existence, also, in complement action of two distinct factors was clearly defined, namely (*a*) combining affinity for the sensitized antigen, and (*b*) toxic action. The chief results of Muir and his co-workers were published together as "Studies on Immunity" (London, 1909); they contributed largely to the foundation of immunology in Great Britain. Thirdly, work on hæmolysis *in vitro* led to investigations on the effects of hæmolytic sera *in vivo*; these enabled new observations to be made, on the storage and utilization of iron (with Shaw Dunn), and on the metabolism of the blood pigments (with J. W. McNee); thus they played a substantial part in the development of Aschoff's concept of the reticulo-endothelial system. Further work followed on the breakdown of hæmoglobin (with Janet Niven) and on the relation of hæmoglobin to the liver cells (with J. S. Young). Fourthly, Muir studied the evolution of cancer of the breast and the spread of cancer cells from the mammary ducts into the epidermis giving rise to Paget's disease of the nipple; his masterly account of these lesions is the most detailed and accurate that has so far been produced.

Muir was elected a Fellow of the Royal Society in 1911 and was awarded a Royal Medal in 1929 for his contributions to immunology. In 1936 he was the first recipient of the Lister Medal who was not himself a surgeon. Muir had an enormous influence on medical teaching both at home and abroad. The "Manual of Bacteriology", first published jointly with James Ritchie in 1897, quickly became the standard work and reached its eleventh edition. In 1924 he added the "Textbook of Pathology", of which the last edition from his own pen was the fifth (1941).

The secret of Muir's greatness in his subject and his profound influence is not easy to define: it appeared to reside essentially in two qualities. In research, he had remarkable judgment and an almost intuitive insight that enabled him to go directly to the heart of the problem. He also carried an aura of intense integrity, and in his presence insincerity and pretentiousness seemed to wither. He was called upon to serve on many committees, both administrative and scientific, and his advice was much sought by universities and Government departments.

To his staff and students Muir was to some extent an enigma. He evoked in them an outstanding affection and loyalty that was entirely uncourted, and in his professional life-time he was something of a legend, many apocryphal tales being told of him. Robert Muir was a highly cultured man, interested in art, literature and music, and he combined these with a keen delight in sport, especially golf and angling. He was knighted in 1934 and was the recipient of many honorary doctorates and fellowships.

D. F. Cappell

Sir Guy Marshall, K.C.M.G., F.R.S.

Sir Guy Anstruther Knox Marshall, director of the Imperial (now Commonwealth) Institute of Entomology during 1913–42, died in London on April 8 at the age of eighty-seven.

Marshall was born in India in 1871 and educated at Charterhouse. Having been unsuccessful in entering the Indian Civil Service, he joined a firm of mining engineers in Salisbury, Southern Rhodesia, in 1895. His intense interest in natural history and acute powers of observation had ample scope in Rhodesia and, in collaboration with the late Sir Edward Poulton, and inspired by him, he published a paper on his observations in the *Proceedings of the Royal Entomological Society of London* of 1902. In 1906 he returned to Great Britain determined to devote his life to entomology, and in 1909 he was appointed scientific secretary to the Entomological Research Committee (Tropical Africa) by the Secretary of State for the Colonies. Almost immediately he started the publication of the now well-known *Bulletin of Entomological Research*, and his energy and enthusiasm were such that in 1913 an Imperial Bureau of Entomology was established. This new organization embraced, and was supported by, all the countries of the British Empire; it was to be a centre of information with two main functions, to issue a monthly periodical giving abstracts of all current literature dealing with noxious insects and to identify injurious insects sent in by workers overseas. The *Review of Applied Entomology*, the abstract journal, first appeared in January 1913 and is now in its forty-seventh volume. At the beginning of 1914 Dr. Sheffield Neave, who had represented the Committee in East Africa since its inception, was appointed assistant director and eventually followed him as director of the Institute in 1942.

The great value of the service that Marshall was building up was quickly recognized by Governments overseas, and first the mycologists of the Commonwealth, and later research workers in other branches, pressed for a similar service. All these services, covering practically all branches of agricultural science, are now grouped together in the organization known as the Commonwealth Agricultural Bureaux.

As adviser on entomological matters to the Colonial Office, he played a very important part between the two World Wars in guiding the development of entomological work in the Colonies and in advising on specific problems. He had a particular interest in tsetse fly research, stemming from his early experience of this pest in Southern Africa. Throughout his long life he never ceased to stimulate, inspire and help entomologists from the Commonwealth, in their work of controlling insect pests. He was a firm believer in commercial companies and insecticide manufacturers employing their own entomologists, and his influence in this direction did much to raise the standard of insecticide products and the service rendered to the public.

Apart from his other activities, Marshall was a leading specialist on the Curculionidae for more than half a century. From 1902 until his death, he published two hundred works on the systematics of weevils, including the descriptions of 2,269 new species of weevils. His major works were "A Monograph of the Genus *Hipporrhinus*" (1904), a volume of "The Fauna of British India" (1916), "Insects of Samoa" (1931), "Entomological Results of the Swedish Expedition 1914 to Burma and British India" (1948) and "The Otiorrhynchine Curculionidae of the tribe Celeuthetini" (1956). He identified the large quantities of weevil material received at the Institute for determination with great promptitude, and he continued to do so after his retirement in 1942, working constantly at the British Museum until a very few weeks before his death.

Marshall received many honours: hon. D.Sc. (Oxon.) 1916; C.M.G. 1920; F.R.S. 1923; knighthood 1930; K.C.M.G. in 1942. He was a corresponding member of the American Academy of Sciences, Philadelphia, honorary member of the Royal Society of New Zealand, of the National Institute of Science, India, of the Entomological Society of Belgium, of the Entomological Society of Russia and an honorary fellow of the Royal Entomological Society of London.

He married in 1933 and is survived by his wife and two stepsons. He will be sadly missed by a host of friends in Great Britain and abroad.

W. J. Hall

Dr. Lynde P. Wheeler

Dr. Lynde P. Wheeler died on February 1, at Roanoke, Virginia, U.S.A., at the age of eighty-four, after a long and active career in physics and radio communication. For many years he was associated with Yale University; he graduated in 1895 and became associate professor of physics during the period 1923–26. In 1918, he also spent some months at the National Bureau of Standards, Washington. On leaving Yale, Dr. Wheeler joined the U.S. Naval Research Laboratory near Washington and, during his ten years service there, he was associated with the application of radio and allied techniques to naval problems. His long experience in radio matters was then made available to the Federal Communications Commission, where he became chief of the Technical Information Section for the period 1936–46. On retirement from the Commission, he became staff-consultant to Pickard and Burns Inc., of Needham, Massachusetts.

Dr. Wheeler was actively associated for many years with the Institute of Radio Engineers (New York), and particularly with its Washington section. He was elected a Fellow of the Institute in 1928, and served as president in 1943.

NEWS and VIEWS

Mathematics at Newcastle upon Tyne:

Prof. W. W. Rogosinski, F.R.S.

PROF. W. W. ROGOSINSKI retires from the chair of pure mathematics at King's College, Newcastle upon Tyne, in the University of Durham in September. He was appointed to the chair at King's College in 1948 after a distinguished career in Germany, Cambridge, Aberdeen and Newcastle, having established an international reputation for his work on Fourier series and functions of a complex variable. During his tenure of the chair he has worked mainly on extremum problems in function spaces. He has written a series of papers concerned with finding minimal representations and maximal points of linear functionals, with applications to extremum problems, systems of linear equations with infinitely many unknowns, generalized moment problems, and other problems of classical analysis. In 1954 he was elected to fellowship of the Royal Society. The Department of Mathematics, and all its activities, have expanded rapidly since 1948, and Prof. Rogosinski has given enthusiastic support and encouragement to all its members. He is held in high esteem and with great affection by his colleagues throughout the College, and he will be greatly missed. His mathematical zeal, however, will be sustained by his appointment to a chair in Denmark.

Prof. F. F. Bonsall

ON the retirement of Prof. W. W. Rogosinski the chair of pure mathematics at King's College, Newcastle upon Tyne, University of Durham, has been filled by the appointment of Mr. F. F. Bonsall. Mr. Bonsall studied at Oxford with an interval for war service. After holding a temporary lectureship in the University of Edinburgh, he was appointed a lecturer in pure mathematics at King's College and became a reader in 1956. His research work has been mainly concerned with partially ordered vector spaces, particularly spectral properties of linear operators mapping the positive cone into itself.

Royal Society Research Appointments

THE Council of the Royal Society has made the following appointments in original scientific research. Royal Society Research Fellowships (Mr. and Mrs. John Jaffé Donation) have been awarded to: Dr. G. Hoyle, of the Department of Zoology, University of Glasgow, to work on excitation/contraction coupling in muscle and nervous mechanism in behaviour of insects, from October 1, 1959, at the Department of Zoology and Institute of Physiology, University of Glasgow; and to Dr. J. Owen, of the Clarendon Laboratory, Oxford, to work on exchange interactions in magnetic systems, from October 1, 1959, at the Clarendon Laboratory, Oxford. Royal Society Research Studentships (Mr. and Mrs. John Jaffé Donation) have been awarded to: Mr. K. L. Manchester, of the Department of Biochemistry, University of Cambridge, to work on the mechanism of the regulation by hormones of protein synthesis, from October 1, 1959, at the Department of Biochemistry, University of Cambridge; and to Dr. M. J. Whelan, of the Crystallographic Laboratory, Cavendish Laboratory, Cambridge, to carry out investigations of metals by transmission electron microscopy, from October 1, 1959, at the Department of Physics, Cavendish Laboratory, Cambridge. John Murray Travelling Studentships in oceanography and limnology for 1959 have been awarded to: Mr. A. D. Ansell, of the Marine Station, Millport, Isle of Cumbrae, to work on problems of the laboratory rearing of bivalve larvæ at the U.S. Fish and Wildlife Laboratory, Milford, Conn.; and to Mr. G. Evans, of the Imperial College of Science and Technology, University of London, to work on marine sediments at sea but based on the Scripps Institute of Oceanography, La Jolla, California.

Rockefeller Institute, New York: Fellowships for Foreign Students

DR. DETLEV W. BRONK, president of the Rockefeller Institute, has announced that the Institute has received a bequest of approximately one million dollars from the estate of the late Sophie D. Fricke, of New York City, who died on March 1, 1958. Miss Fricke was born in Jersey City, but lived most of her life in New York where she was confidential secretary to many prominent business executives. Through wise investment of her personal savings, she created the fortune which she left for the furtherance of human welfare through support of science. The Trustees of the Institute, which has recently been transformed into a postgraduate university, have authorized use of the income from the Fricke fund for the triple purposes of fostering international understanding, training scientists of exceptional promise, and supporting significant research. To this end, four distinguished research fellowships will be awarded each year to young scientists in Britain, France, Denmark and Sweden for study and investigation at the Institute. The Fellows will be appointed by the Royal Society of London, the Paris Academy of Sciences, the Royal Danish Academy of Sciences and Letters and the Swedish Royal Academy of Sciences. Each Fellow will carry the designation of his sponsoring society. For example, the Fellow from Britain will be known as the Sophie Fricke Royal Society Research Fellow in the Rockefeller Institute. Each of the Sophie Fricke Fellows will receive an annual stipend of 10,000 dollars with an additional 1,000 dollars for travel in the United States.

"The objective of these fellowships," said Dr. Bronk, "is to foster closer relations between American scientists and their colleagues from abroad. It is our intent that the Fellows be young men and women of exceptional promise who are likely to be leaders in science in their respective countries and will, therefore, ultimately be appointed to distinguished posts in their native lands. Having spent one or two years in the United States under exceptionally favourable circumstances before assuming posts of responsibility at home, these men and women will be in an unusually favourable position to develop the associations with American scientists begun while at the Rockefeller Institute. All the facilities of the Institute and the advice and guidance of the Institute's distinguished faculty will be available to the Fellows; they will be free to work on problems of their own choosing or they may collaborate with one or more members of the Institute Faculty."

Sir K. S. Krishnan, F.R.S.

On December 3, 1958, Sir K. S. Krishnan celebrated his sixtieth birthday, and to commemorate this event the contents of the December issue of the *Journal of Scientific and Industrial Research* included two special features. The first is a reprint of the article describing Prof. Krishnan's distinguished scientific career which Prof. K. R. Ramanathan contributed to the Souvenir Volume published by Prof. Krishnan's Sixtieth Birthday Celebrations Committee, New Delhi. The second consists of a 110-page supplement containing reports of the work carried out under the auspices of the Indian National Committee for the International Geophysical Year, 1957–58, of which Prof. Krishnan was the chairman and active director. A brief foreword to the supplement is followed by two short articles entitled "Sir K. S. Krishnan and the International Geophysical Year" and "Space Exploration—An Achievement of the I.G.Y.", by Profs. Sydney Chapman and L. V. Berkner, respectively, and sections devoted to meteorology, geomagnetism, ionosphere, solar activity, cosmic rays, latitudes and longitudes, glaciology, oceanography, rockets and satellites, and seismology, containing twenty-four reports in all. India took part in every one of the fourteen divisions of the international programme and maintained, in addition to a large network of meteorological stations, about sixty other observation stations distributed all over the country. India's geographical position and the vast area of the country render its particular contributions to the International Geophysical Year programme of special significance, and the detailed results given in the reports are a valuable addition to geophysical data and a stimulus to the conquest of space.

The Microbiological Research Establishment

In reply to a question regarding the work of the Microbiological Research Establishment in the House of Commons on May 4, the Minister of Supply, Mr. A. Jones, said that the work of the Establishment is of much wider interest than its aspects relating to the defence programme and involves fundamental studies in microbiology which have applications in preventive medicine. Mr. Jones instanced the development and production of a completely safe vaccine against anthrax and the production of raw material for Asian influenza virus vaccine used in the 1957–58 epidemic. During 1958 more than 80 articles were published by members of the staff in medical and scientific periodicals, and biological materials were regularly provided for use in microbiological departments engaged in medical research at universities and other institutions. In reply to a further question, the Minister said that it is the Establishment's function to study the problem of biological warfare and much progress has been made. It is not now thought that botulinus toxin would be an effective agent, and efficient protective measures have also been developed. Our ability to assess and encounter the threat has increased with the growth of our knowledge of the subject from research, but much still remains to be done.

Mathematics in American Secondary Schools

"An Emerging Programme of Secondary School Mathematics", the Inglis Lecture for 1958 (pp. viii + 44. Cambridge, Mass.: Harvard University Press; London: Oxford University Press, 1959. 7*s.* 6*d.* net), is an account, given by Prof. Max Beberman, of a diagnostic experiment in teaching method which has been in operation since 1952 under the auspices of the University of Illinois. The investigation is designed to establish whether mathematicians can formulate a course of instruction for pupils, and a programme of training for teachers, so that the subject may have a greater appeal to the average child. The lecture postulates two fundamental principles for a course now being applied to the last four years (age range about 13–17) in twelve American high schools. The first principle, the need for precision in language, is exemplified here by the ability to appreciate the difference between the figure '3', the name 'three' which we apply to this figure, and the 'number' three which is the *class* of sets of three things. The second is the necessity for discovery as an aid in understanding the nature of mathematics; examples relate to directed numbers, the solution of equations and inequations ($|2x + 1| < 7$), the manipulation of algebraic expressions and the 'ordered pair' approach to analytical geometry. In this account there is insufficient detail to give the reader a convincing understanding of the effectiveness of this actual programme. Enough is said, however, to establish beyond doubt that only by such experiments in training and teaching under pilot conditions can the content of the syllabus in school mathematics be settled with any real certainty.

Language, Literature and Science

Prof. A. Norman Jeffares's inaugural lecture in the chair of English at the University of Leeds has been published by the University (pp. i + 24. Leeds: The University Press, 1959. 2*s.* 6*d.*). It is a matter for satisfaction and congratulation that Prof. Jeffares has made a plea for the presentation of the best scientific writing as literature. On one hand, the scientist should consider the clearest and most cogent method of presenting his knowledge to those who are not workers in scientific fields; and on the other, the arts student must endeavour to understand the significance of the aims and methods of, and the changes in the world wrought by, science. "Humanism must include science: a refusal on the part of the man trained in arts to launch himself into the sea of scientific thought is as dangerous for us as any obfuscation of that thought on the part of a scientist untrained in the technique of using his own language —'Science is or ought to be poetry and poetry is knowledge, and the humanity of the future will not divide life but unite it'. But the humanism of the future depends upon our reading of the literature of both humanism and science, upon our listening to those who conserve, add to or modify both these traditions of humanism and science, and upon our own writing and speaking good English, the existence of which is the common bond between humanism and science."

International Federation of Societies of Cosmetic Chemists

A meeting took place in the rooms of the Chemical Society, Burlington House, Piccadilly, London, on April 15, when representatives of eight countries met to discuss the formation of an International Federation of Societies of Cosmetic Chemists. This Federation would link together the various autonomous national societies into an international body, capable of acting in such fields as international standards, establishment of the professional status of the cosmetic scientist, publication of bulletins, abstracts and reviews on cosmetic science, to name only a few. The countries represented on this occasion were: Belgium, Denmark, France, Germany, Great Britain, Norway, Sweden and the United States. Agreement was reached on a provisional constitution. The delegates are now returning to report to their national societies, and as soon as possible a second council meeting will be held to draw up a final constitution. A provisional secretariat has been established in London (2 Lovers Walk, London, N.3), but the final headquarters have yet to be agreed.

Technical Assistance under the Baghdad Pact

In a written answer in the House of Commons on April 9, Mr. R. Allen, Joint Under-Secretary of State for Foreign Affairs, stated that at the sixth session of the Baghdad Pact Economic Committee in January 1959, the Government announced its intention to make available £850,000 per annum for technical assistance under the Baghdad Pact. This will be used for the supply of equipment and technical experts to Turkey, Iran and Pakistan and to provide training in the United Kingdom for nationals of those countries. In addition, the Government had contributed the equipment for the Nuclear Training Centre in Baghdad as well as some of the staff and running costs. Negotiations between the Pact Organization and the Iraqi authorities for the disposal of this equipment had not yet been completed.

Scottish Technical Education Consultative Council

In a written answer in the House of Commons on May 1 the Secretary of State for Scotland, Mr. J. Mackay, announced that the new consultative body on vocational further education would be known as the Scottish Technical Education Consultative Council; its terms of reference would be "to secure the widest possible measure of consultation on vocational further education in Scotland between employers, employees and those responsible for its provision, and to advise on, and generally to promote, the development of such education". Its chairman will be Mr. E. P. Hudson and its vice-chairman, Sir David Anderson.

Government Chemist's Department

It was announced by Mr. J. E. S. Simon, Financial Secretary to the Treasury, in a written answer in the House of Commons on May 4, that the Government agrees with the Linstead Committee that the arrangement whereby the Chancellor of the Exchequer is responsible for the Government Chemist's Department is inappropriate in the present organization of Government scientific work. As from July 1 next, Ministerial responsibility for the Department will be transferred to the Lord President of the Council, and the Department will be placed in the charge of the Council for Scientific and Industrial Research.

Building Research

In answer to a question in the House of Commons on May 5, the Minister of Works, Mr. H. Molson, said that the Government has for some time recognized that there is room for improvement in the co-ordination of building research, and it has therefore been decided to place all such research under the Department of Scientific and Industrial Research. He is not therefore re-appointing his Advisory Council on Building Research and Development, and in its place there would be a Standing Conference on Building Research under the ægis of the Lord President of the Council. The dissemination of technical information will remain his responsibility and he is discussing with the industry the many problems involved in providing rapid facilities for this purpose.

Journal of Biochemical and Microbiological Technology and Engineering

It is generally recognized that chemistry imposes certain special conditions on the technologists and engineers who work in chemical industry. Biology, too, possesses its own characteristics which must be understood by people who are proposing to use living cells for practical purposes in biological industry. It is with this in mind that three editors, two from the University of London and one from Columbia University, New York, assisted by an advisory board of sixteen drawn from Australia, India, Ireland, Italy, The Netherlands, Sweden, Switzerland, the United Kingdom and the United States, have brought out this new journal. The first number (*Journal of Biochemical and Microbiological Technology and Engineering*, 1, No. 1; February 1959. Pp. 127. Published quarterly: subscription, covering one volume annually, £5 15*s*., including postage; outside the United Kingdom, 15.50 dollars. New York and London: Interscience Publishers, Inc., 1959) contains nine papers which nicely illustrate the kind of topics with which the publication is intended to deal. For example, an American contribution describes the separation of proteins by means of foam; N. W. Pirie reviews the principles employed in different types of presses, filters and centrifuges by which fluids may be separated from fibrous pulps on a large scale; and the British Flour-Millers Research Association presents a paper on the use of air classification as a means of varying the protein content of flour. Besides these, there are reports on equipment for the culture of algae and of micro-organisms of diverse kinds for various purposes, on the destruction of moulds by irradiation, on the evaluation of microbiological nutrients and on means for the removal of algae from drinking water. Pure and applied science must always be inextricably mixed. Neither physicists nor chemists could achieve their modern triumphs without their technologies. The present journal can usefully inform biologists about theirs.

Locusts and Atmospheric Turbulence

In a paper entitled "Flying Locusts and Atmospheric Turbulence" (*Quart. J. Roy. Meteor. Soc.*, 84, 334; 1958), Dr. R. C. Rainey describes the relation between the structures of the lower atmosphere and of locust swarms over eastern Africa. It is found that, in a convectively unstable atmosphere of very high lapse-rate of temperature, the locusts are carried high into the air in the convection currents. They are spread out over a considerable depth rather like a cumulus cloud so that there is a nearly clear space for some distance above the ground, while the top of the swarm approaches the limit of the region of high lapse-rate at 1–2 km. above the surface. During stable (isothermal) conditions, on the other hand, the swarm forms a thin layer at a height of a few tens of metres above the ground. In such conditions, locusts frequently settle on the ground, and take off again as the swarm progresses. The locust swarm is not, however, merely carried along by the air and dispersed by turbulence as though it were a cloud of dust particles. Evidence is presented to show that, even in highly convective air, the swarms persist as swarms. The facts presented in the paper are of importance in selecting suitable occasions for spraying locust swarms with insecticide and also, to an extent restricted by the little-understood coherency property of a swarm, in the study of convection currents. The paper contains two photographs vividly illustrating the difference between locust swarms in convective and stable atmospheres.

New Guinea

A RECENT issue of the *Australian Museum Magazine* is devoted almost entirely to New Guinea (12, No. 12). The physical geography is described by D. F. McMichael and the geology by G. A. U. Stanley. J. S. Womersley discusses the vegetation of the island, while other contributors provide details about the mammals, birds, fishes and insects. Until the early 1930's it was thought that the central region of New Guinea was uninhabited and uninhabitable. Since that time it has become known that about 600,000 people live in the Australian territories alone. These, and others of the many different types of natives, are described by A. P. Elkin. This issue is also of interest for its reference to the discovery of a rare animal in Australia, the potoroo (*Potorous tridactylus*). This animal, which is related to the rat-kangaroos, is now rare in New South Wales, not having been recorded in the State since 1913. It is still common in Tasmania. The specimen obtained by the Museum was killed by a dog near Gosford, New South Wales.

"Chlorothiazid in Diabetes Insipidus"

Drs. John D. Crawford and G. C. Kennedy write: "We have recently reported that chlorothiazide has an antidiuretic action in experimental and clinical diabetes insipidus, both of the pituitary deficiency and nephrogenic varieties (*Nature*, March 28, p. 891). It has been brought to our notice that Drs. H. Reerink, Eveline E. Brongers and H. Schouten reported on the use of chlorothiazide in the treatment of three cases of nephrogenic diabetes insipidus before the Dutch Organization for Paediatrics at Eindhoven on June 15, 1958. Their rationale was 'to impede the (renal) tubular reabsorption of Na and Cl in order to induce the excretion of these ions into the urine for the purpose of regulating the level of these electrolytes in the blood'. We would like to acknowledge their priority in the successful use of chlorothiazide for amelioration of symptoms in nephrogenic diabetes insipidus".

Announcements

THE Challenger Society is prepared to make small grants for research in marine biology or oceanography at a recognized laboratory during the year June 1959–60. Applications, accompanied by details of the proposed research, should reach the Hon. Secretary, Challenger Society, National Institute of Oceanography, Wormley, near Godalming, Surrey, not later than May 30.

FOR a number of years the directors of the Associations of Chemical Manufacturers in western Europe have found it useful to meet from time to time to examine together questions of common interest. In view of the number and scope of the problems facing the chemical industries of these countries at the present time, the Austrian, Belgian, British, Dutch, French, German, Italian, Swedish and Swiss Chemical Manufacturers Associations have decided to improve their collaboration and contacts by setting up a Centre Européen des Federations de l'Industrie Chimique, the secretarial services of which are to be entrusted to the Swiss Association in Zurich.

A MEETING of the members of the Co-operative Research Project on Trace Elements of the United Nations Food and Agriculture Organization, organized by An Foras Talúntais (The Agricultural Institute, 33 Merrion Road, Dublin), will be held in Dublin during May 20–23. The results of the recent survey of trace-element research problems made by Prof. T. Wallace of Long Ashton Research Station, Bristol, co-ordinator of the project, will be discussed at the meeting. Other subjects for discussion will be the evaluation of trace-element deficiencies in Europe; the status of research on trace elements; methods of trace-element analysis and methods of strengthening research and collaboration on trace elements.

THE Food and Agriculture Organization of the United Nations will offer ten or twelve André Mayer Fellowships in 1959. These awards will be made in the following two groups: (*A*) *Research*. For unusually promising persons with research experience behind them who would offer a guarantee to carry out independent research work. (*B*) *Research training*. For younger and promising individuals who have demonstrated an inclination towards, and an aptitude for, research work. The subjects presented must be related to the Organization's activities. Further information can be obtained from the Secretariat of the Food and Agriculture Organization, National Committee for the United Kingdom, Ministry of Agriculture, Fisheries and Food, Whitehall Place (East Block), London, S.W.1.

THE Summer Meeting of the Photoelectric Spectrometry Group will be held in Nottingham on June 12. Further information can be obtained from K. A. Macdonald, Unicam Instruments, Ltd., Arbury Works, Cambridge.

THE seventeenth International Congress of Pure and Applied Chemistry will be held in Munich during August 30–September 6. Further information can be obtained from Dr. R. Morf, c/o Sandoz, S.A., Basle 13, Switzerland.

THE Scientific and Technical Group of the Royal Photographic Society is holding a symposium on Photography in the International Geophysical Year on June 6 in the Adam House Theatre, Chambers Street, Edinburgh 1. Further information can be obtained from Mr. D. Brownbill, Technical Service Department, Ilford, Ltd., Ilford, Essex.

THE Eastern New York Chapter of the American Society for Metals will sponsor a conference on the Fracture of Engineering Materials during August 23–25 at the Rensselaer Polytechnic Institute, Troy, New York. Further information can be obtained from Richard W. Hardt, General Engineering Laboratory, General Electric Company, 1 River Road, Schenectady, N.Y.

THE summer courses of the Italian Physical Society's International School of Physics will be held in the Villa Monastero, Varenna, during June 15–September 15. Courses will be held on thermodynamics of irreversible processes; weak interactions; solar radio-astronomy; physics of plasma; experiments and techniques. Further information can be obtained from the Società Italiana di Fisica, Via Saldini, 50, Milano.

THE FONTÉCHEVADE SKULLS AND THE ORIGIN OF *HOMO SAPIENS*

THE long-awaited full report on the human remains from the Fontéchevade Cave (Charente) in south-western France, where in August 1947 the fragmentary skulls of two individuals associated with a Tayacian industry were discovered by Mlle G. Henri-Martin, has now been published*. The palæontological and chemical evidence of their age, taken in conjunction with that of archæology and stratigraphy, points to an early part of the Riss–Würm interglacial—some authorities favour the Riss glaciation itself—or a time preceding the advent of the Mousterian culture associated with Neanderthal man. Fontéchevade I consists of a small piece of the glabellar region of the frontal bone, and Fontéchevade II, which has been affected by burning, of almost the whole left parietal, the upper half of the right parietal, and the upper portion of the frontal.

Prof. H.-V. Vallois concludes that Fontéchevade I belonged to an adult subject of probably female sex. It is slightly thicker than the corresponding region in modern European frontals and does not show any marked development of the glabella, its most characteristic feature for so ancient a specimen being the complete absence of a supra-orbital torus. His study of Fontéchevade II is lengthy and thorough, involving comparisons of separate characters with those of Lower and Middle Palæolithic fossil skulls from Europe and western Asia. In this the defective state of the specimen necessitated the making of assumptions in the reconstruction of certain missing regions. According to Prof. Vallois, its owner was probably male and 50–60 years old at the time of death. The cranial capacity he determines from one of the Lee–Pearson reconstruction formulæ based on calvarial length, breadth, and auricular height (measured from the biporial axis to the apex and not, as erroneously stated in Rudolf Martin's "Lehrbuch der Anthropologie", to the bregma), less 50 cm.^{3} as an allowance for exceptional thickness of bone, to be 1,470 cm.^{3}. A preferable formula would seem to be the corresponding one of Hooke[1], used by Morant to estimate the capacity of the Swanscombe skull[2], which, with the same deduction as before, yields an even higher figure of about 1,550 cm.^{3} for Fontéchevade II. However, the arbitrary nature of such estimates from incomplete material must be stressed. The dimensions of the skull are in any event considerable. As seen from above, the vault is pentagonal, the greatest breadth is situated at a low level, and the biasterionic diameter has a high value. The frontal bone, like that of Fontéchevade I, apparently lacks a torus and has no post-orbital constriction. There is an absence of parietal foramina, which it shares with the majority of the more ancient representatives of fossil man.

The fourth chapter of Prof. Vallois's monograph is an attempt to assess the taxonomic position of the Fontéchevade Tayacians, whom he now compares *en bloc* first with three different 'Neanderthal' groups, namely, the 'classic' Neanderthals of the last or Würm glaciation in Europe, the pre-Neanderthals of the same continent, including the Ehringsdorf and the two Saccopastore skulls, all from the Riss–Würm interglacial, and the Steinheim skull, probably of Rissian age, and the Palestinian Neanderthaloids, dating from the Riss–Würm or the Würm I–II interstadial; then with European fossil *Homo sapiens*; and finally with the Swanscombe skull from the Mindel–Riss. So far as the classic Neanderthals are concerned, Prof. Vallois points out numerous distinctions between these and the Fontéchevade skulls, a categorical one being the form of the forehead and in particular the absence of a supra-orbital torus in the Tayacians, a feature also separating them from the remaining two 'Neanderthal' groups treated by him. He replies to critics who, broadly speaking, are unconvinced that the Fontéchevade fragments can be distinguished in any definitive way from the pre-Neanderthals of Europe, and stresses the close resemblance that exists between Fontéchevade II and the Swanscombe skull.

Prof. Vallois then devotes a substantial portion of his text to the 'Presapiens' concept, that is to say, the reasons in favour of the existence of a line of fossil men who, while more ancient than the classic Neanderthals, nevertheless differ from them and from the pre-Neanderthals in the complete absence of a supra-orbital torus and display in this and other characters an approach to *Homo sapiens*. He discusses in turn the development of this concept and the claims for various finds to be included in the 'Presapiens' category. Briefly, only three individuals qualify, the two from Fontéchevade and the Swanscombe skull, of which the frontal bone is missing. He next considers the argument that the Swanscombe skull, if its frontal were present, could have been furnished with a torus as developed as that of the almost contemporary Steinheim skull, a suggestion first made by Morant, who pointed out the similarity in bone thickness and in the conformation of the occiput between Swanscombe and Steinheim. A provisional diagnosis of 'Presapiens', based on the traits of the Fontéchevade and Swanscombe skulls, is followed by the statement that it represents a primitive form of *Homo sapiens*, from which 'Presapiens' was probably not specifically distinct and of which it ought logically to be considered as an initial stage.

In his fifth chapter Prof. Vallois reviews the theories of the origin of *Homo sapiens*, which he classes under three main heads: (1) direct derivation from classic Neanderthal man, (2) derivation from pre-Neanderthals, and (3) derivation from a source independent of either, that of 'Presapiens'. The essentials of the case for each are set forth with the lucidity and encyclopædic knowledge of which the author is so remarkable an exponent. Naturally enough, the solution that he himself favours is the third one, that which envisages a separation of the lines leading respectively to *Homo sapiens* and to the classic Neanderthals in the Lower Pleistocene and perhaps no earlier than its post-Villafranchian phase.

Presented though they are with the skill and authority that Prof. Vallois commands, the arguments in support of the 'Presapiens' thesis, as expounded by him, have had a mixed reception among students of human palæontology. Thus the veteran Prof. Sergio Sergi, in a paper devoted to the Swanscombe and Fontéchevade remains[3], emphasizes the uncertainty of an adequate morphological diagnosis from them owing to their incompleteness. While acknowledging that they possess some traits in common with *Homo sapiens* such as the absence of a supra-orbital torus in Fontéchevade and certain metrical features in Swanscombe, he believes that their platycephaly, great biasterionic diameters, and posterior expansion of the base of the parietals are structurally archaic features the importance of which has been underestimated. In other words, it is not possible to recognize different pre-Neanderthal and 'Presapiens' groups much before the Würm. For Sir Wilfrid Le Gros Clark the morphological traits of Swanscombe and Fontéchevade as well as those of other European fossils, for example, Steinheim, Ehringsdorf, Krapina and Saccopastore, do not justify their specific separation from *Homo sapiens*[4]. This view, then, while acknowledging the sapient features of Swanscombe and Fontéchevade, does not differentiate them taxonomically from forms which Prof. Vallois would classify as pre-Neanderthals, and it regards classic Neanderthal man as comprising an aberrant evolutionary line which left the precursors of modern man when they had already attained a stage at which they were indistinguishable from *Homo sapiens*.

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* Archives de l'Institut de Paléontologie Humaine, Paris. Mémoire 29: La Grotte de Fontéchevade. Deuxième partie: Anthropologie. Par Henri-V. Vallois. Troisième partie: Géologie et Paléontologie. Par H. Alimen, C. Arambourg et A. Schreuder, avec la collaboration de G. Henri-Martin, J. Berlioz et J. Bouchud. Pp. 262+6 planches. (Paris: Masson et Cie., 1958.)

J. C. TREVOR

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[1] *Biometrika*, **18**, 1 (1926).

[2] *J. Roy. Anthrop. Inst.*, **68**, 67 (1938).

[3] *Riv. Antrop.*, **40**, 65 (1953).

[4] "The Fossil Evidence for Human Evolution" (Chicago, 1955).

PLANT ECOLOGY OF ANCIENT PERIODS

THREE palæobotanists contributed papers to a symposium on palæoecology held at the Linnæan Society on March 19. They agreed on a wide definition of ecology, being ready to include almost anything that could be learnt from plant fossils, apart from their taxonomy and their morphology. After that, each speaker went his own way and confined himself to material he had studied in both the field and laboratory.

Dr. Kathleen Chesters spoke about the Tertiary floras of the coastal parts of Kent, Sussex, Hampshire, Dorset and Devon. She emphasized how difficult collecting has now become in this stretch of coast; and also dealt with the cliffs of Mull, where one can do little without explosives (Starkie Gardener, the pioneer, used dynamite). She dealt mainly with the nature and validity of evidence; apart from deductions from geology and from fossil animals, we have two main kinds of evidence from plants.

First, there is ecological form and ecological anatomy. The plant world of the Tertiary seems so like our own, and plants appear to have changed so little that we can reasonably use arguments based on the modern plant world. For example, we know that the proportion of trees with leaves (or leaflets) with entire margins increases from cool climates to the tropics. Then, also, leaves with drip tips are much commoner in rainy than in dry climates. Growth rings in wood indicate seasonal growth, and to-day, usually a winter resting season. All this evidence is available without a specific or generic determination, but where there is such determination it is possible and legitimate to inquire in what climatic zones most of the genera flourish to-day; or even in what country they are found. Where both lines of evidence coincide, as in general they do, one has impressive evidence. Dr. Chesters briefly made a case for likening the Eocene floras to those of Malaya, but the Mull flora (not yet securely dated) to the warm temperate floras of China and Japan.

Prof. T. M. Harris (Reading) said that the corresponding arguments were largely useless in the Jurassic because nothing like the Jurassic flora exists anywhere on earth. A quarter of the species belong to extinct families and the rest to relic families (like *Gingko* and *Thyrsopteris* and *Matonia*). Gymnosperm leaves are too different from those of angiosperms to allow reasonable comparison of their ecological form, and he suggested that the more tender ones were simply deciduous and the tough ones evergreen. He could not answer reasonable questions about past climates, but could only supply unexpected ecological crumbs, such as that forest fire was widespread and rather frequent in the Jurassic.

In the Yorkshire Deltaic flora the frequency of ferns might indicate a humid atmosphere, but the rarity of epiphytes rather suggests dryness. He showed that the Delta included three floras, swamps of *Equisetum*, often preserved intact; trees and herbs of the river banks represented by detached leaves but nowhere preserved as they grew, and, finally, tiny plant fragments. These last are the most varied, numerous and widespread and may represent floras of inland habitats washed down by occasional floods.

Dr. W. S. Lacey (Bangor) dealt with his recent experiences when collecting in the Karoo series of the Upper Zambezi in Southern Rhodesia. He drew more on geological evidence than the previous speakers. This great series of inland origin extends from the Upper Carboniferous to the Jurassic. It begins, as in South Africa, with Dwyka glacial deposits (tillites and varved clays), but farther north in Nyasaland there is no glacial deposit but only torrent-carried boulders.

The earliest floras are too little known to be useful, but the succeeding rich flora of Upper Wankie sandstone and the 40-ft. thick coal seam are taken to indicate good conditions for plant growth. The admixture of *Glossopteris*, *Gangamopteris* and of Northern (mostly European) Upper Carboniferous or Lower Permian species was also held to indicate warmth, since they are supposed to have lived in a very warm climate in Europe. Later stages, though still with a rich *Glossopteris* flora, have lost both the genus *Gangamopteris* and the Northern species. They are followed by Triassic floras with *Dicroidium* and the conifer-like *Dadoxylon* the growth rings of which seem significant. Still later there are freshwater concretionary limestones which may indicate evaporating lakes, and finally extensive fossil sand dunes indicating a hot, dry desert.

Dr. Lacey said he hesitated to regard *Gangamopteris* as an indicator of a glacial or even cold climate. He thought the whole sequence indicated a progressive warming and desiccation of the climate, though interrupted by seasonal torrential rains. At several stages no plants are known, but their presence is indicated by herbivorous reptiles, and the appearance of Crustacea characteristic of the European Carboniferous may indicate considerable warmth in the later stages.

In the discussion (which proved to have needed more time than was allotted) many observations were made. Dr. Chesters confirmed the existence of mangroves in the English Eocene and also stated that epiphytes had still not been found. There were apparently opposed statements about the rate of decay of plant remains in tropical muds which called for a series of experiments to find out the truth. One of the Upper Karoo plants (*Lepidopteris stormbergensis*) was compared with a modern waterside aquatic herb, with which it agrees in that some small leaves, presumed to be lower ones, have more numerous stomata above than below. Its other leaves are normal. Others pointed out that limestones are forming to-day in East African lakes quite apart from evaporation of the water.

Dr. Hamshaw Thomas ended the discussion fittingly by suggesting that the early floras, like none on earth, grew in climates like none on earth to-day, but just how these climates differed he left us to ponder.

TOM M. HARRIS

WEATHER MODIFICATION IN THE UNITED STATES

THE National Science Foundation has recently initiated a programme in which 1,130,000 dollars will be distributed in thirteen grants for laboratory research, field experiments and conferences on meteorological methods directed toward modification of weather. The programme aims at an intensive study of the scientific basis of weather control, through the support of scientists working in cloud physics and allied fields.

Seven of the grants will make extensive use of experiments in the field to study the formation and characteristics of clouds, and possible changes in clouds induced by man.

Horace R. Byers and Roscoe R. Braham of the Department of Meteorology, University of Chicago, have received a grant of 114,300 dollars for a study of the physical effects of silver iodide seeding over the Great Plains. Cloud seeding in mountainous areas of the Pacific coast appears to result in measurable increases in precipitation. Over the flat terrain of the Great Plains, however, positive results have not been shown. This project will therefore release silver iodide nuclei from aircraft and investigate the resultant physical changes in the clouds themselves, rather than attempt to measure statistical departures in precipitation.

A. Richard Kassander, Louis J. Battan, and James E. McDonald of the Institute of Atmospheric Physics, University of Arizona, have received a grant of 161,800 dollars to study the physics of clouds and of cloud modification. In recent cloud-seeding experiments it was discovered that mean rainfall was approximately 30 per cent higher on seeded than on non-seeded days, and lightning flashes were about nine times more numerous on seeded days. These investigations will continue in an attempt to improve knowledge of the development of clouds, precipitation and electrification.

Robert D. Elliott of Aerometric Research, Inc., Goleta, California, will conduct an investigation of precipitation processes and efficiency of Pacific coast storms with a grant of 90,500 dollars. Statistical data on west coast storms are already available from the Statistical Laboratory of the University of California at Berkeley, and elsewhere. An intensive effort will now be made to obtain physical data on west coast storms, including water content, nuclei number, potential gradient, and standard meteorological parameters. This will then be combined with the statistical data to develop, it is hoped, a complete model of a west coast storm.

Dwight B. Kline of the United States Weather Bureau, Department of Commerce, will direct an 18-month programme with a grant of 68,900 dollars, on synoptic observations and studies of freezing nuclei anomalies. It has been observed that about 30 days after known meteor showers on the Earth, a peak is reached in the number of freezing nuclei in clouds, in widely separated geographical locations. Other apparent coincidences between meteor showers and freezing nuclei have been noted. The U.S. Weather Bureau will conduct a systematic collection of results on freezing nuclei taken at widely scattered places at the same time. It is hoped that definitive information on the effects of meteoric dust on cloud nuclei can be obtained from this study.

The Atmospheric Research Group of Pasadena, California, will receive a 57,100 dollar grant to conduct field studies in cloud physics related to nucleation, hydrometeor development, electrification, and cloud dynamics. Field studies of small, 'simple' clouds will be conducted to investigate the effects of time, temperature, humidity, and drop-size on nucleation. Cloud seeding will be used as a research tool, most of the field measurements being carried on in the region of Flagstaff, Arizona.

The National Science Foundation has transferred 50,000 dollars to the Office of Naval Research in support of cloud electrification studies by A. D. Little, Inc., under the direction of Bernard Vonnegut. This work involves studies of the precipitation process and the processes at work in the electrification of thunderstorms.

Meteorology Research, Inc., will receive, subject to satisfactory completion of negotiations, a 40,000 dollar contract for two-year cloud-physics studies at Santa Barbara, under the direction of Paul MacCready, using radar to describe individual storms in great detail, to determine differences between storms, and formulate hypotheses on the relative seedability of various storms.

A laboratory project will be carried out in the Department of Meteorology of the University of Chicago, where Horace R. Byers has received a three-year grant of 383,700 dollars for research in cloud physics, covering the factors believed to be important in precipitation mechanisms: particles and nuclei, ice nucleation processes, and the growth of ice crystals and water droplets.

Two grants have been made for statistical evaluation of cloud-seeding experiments. J. Neyman of the University of California at Berkeley will direct a group in the Statistical Laboratory on randomized cloud-seeding experiment under a two-year grant of 64,900 dollars. Such experiments have been conducted for two years in Santa Barbara and Ventura counties, and will be continued. The data available will be subjected to statistical scrutiny independent of any *a priori* hypotheses concerning the distribution of rainfall, using non-parametric statistical methods with the aid of a high-speed computer.

Max A. Woodbury of the Department of Mathematics, New York University, will make a two-year study of the statistical evaluation of weather modification with a grant of 58,800 dollars.

Three grants in support of conferences have also been made. The American Geophysical Union has received 25,000 dollars for a conference on "Mechanisms of Precipitation Formation". The National Academy of Sciences–National Research Council has received 10,000 dollars for a conference on the "Design and Conduct of Research Programmes in Weather Modification", under the direction of S. S. Wilks of the Division of Mathematics. The Foundation for Instrumentation Education and Research received 5,100 dollars for a conference on "Instrumentation for Cloud and Weather Modification".

PERSONNEL MANAGEMENT IN PERSPECTIVE

An inquiry into the reasons why modern personnel management is experiencing a crisis in its development, and why it is not producing better work through happier employees, has recently been made by Col. L. Urwick*. The major weakness in modern personnel management is, he suggests, its lack of integration into the organizational structure of businesses. There are many historical reasons for this trend and it needs urgent remedying. The corrective needs to be introduced at the very top of industry, by the leaders of business themselves.

The final strength of a business is no more than the collective strength of the individuals composing it. This has been known for years and in the past two decades business has invested millions of pounds in various schemes of personnel management. The expected results have not been achieved. The work-force remains obstinately unmoved, and management itself has its doubts. One reason is that business still looks on its employees as 'economic men' seeking exclusively economic objectives, whereas in reality social objectives are more important to most employees. Another reason is that employees are seen as individuals and not as members of a social group. The effort of personnel management is not directed towards achieving high morale through the social group. The test of a good personnel policy is high morale, a matter not so much of doing things materially for employees, as of stimulating them to achieve something together. High morale requires, above all, leadership from the chief of the enterprise.

Historical trends have weakened the leadership content in personnel management. Personnel activities have become something 'tacked on to' a business because of the need for specialization, and this has prevented the personnel officer from obtaining the authority which should have accompanied his specialized responsibility. The solution is to make the 'line' manager at every level more directly responsible for personnel activities, using the personnel officer more fully for advice.

'Line' managers, especially at the heads of businesses, have found themselves overloaded in attempting to discharge their personnel responsibilities. The solution is to develop the use of general staff officers who can relieve their chiefs of details in all their functions. The possibilities here have long been understood by the Armed Services but are still not exploited in business.

Personnel management has suffered from the growing pains of the new kind of management, which acknowledges a much greater social responsibility, but is fitful in its efforts to shoulder the new burdens. Personnel men were given sometimes too much authority, sometimes too little. The solution is patient, sustained and prudent effort over many years by business leaders to get a personnel policy working well within their organization.

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* Institute of Personnel Management. Occasional Papers, No. 13: Personnel Management in Perspective—Suggestions on the Correct Place of Personnel Activities in Business Organization. By L. Urwick. Pp. 23. (London: Institute of Personnel Management, 1959.) 4s.

HÆMATOLOGY

A NUMBER of the *British Medical Bulletin* (15, No. 1; 1959) has attempted to review some of the many important advances that have been made in hæmatology in the past few years. This, in a series of fourteen articles, the contributors have done in a most stimulating and readable manner. The subject-matter covered includes the deficiency anæmias, the chemistry of normal and abnormal hæmoglobins and their inheritance, hæmolytic anæmias, the leukæmias, the life-history of the lymphocytes and bone marrow culture.

Many of these reviews are particularly stimulating. The description of the life-history of the lymphocytes, cells which hitherto have been somewhat mysterious cells, shows that the usual concepts of their life within the body must be reconsidered.

Normal hæmoglobin synthesis is presented in contrast to a description of the chemistry of the abnormal hæmoglobins. Modern methods of electrophoresis and chromatography have shown that the sole difference between normal adult and sickle-cell hæmoglobin lies in the substitution of one amino-acid for another in one of their constituent peptides. Similarly, the exact defects in other abnormal hæmoglobins are being elucidated.

The alterations of red cell structure in other forms of hæmolytic anæmias are described where (either due to inherited or acquired defects) chemical changes in the lipoid, protein, glutathione or glycolytic systems can be demonstrated. Other aspects of the hæmolytic mechanisms are covered by reviews of the latest modifications in our knowledge of the serology of acquired hæmolytic anæmias, and descriptions of the methods of determining red cell survival and the sites of red cell sequestration using radioactive chromium-51.

The topical problem of the factors that are implicated in the causation of leukæmia are discussed together with the latest methods of treatment in chronic leukæmia.

In these articles faults and omissions are few, but the effects of ionizing radiation in the causation of leukæmia could have been discussed more fully in view of the current national and medical interest in this subject. The reader is left in some doubt as to the exact percentage of fœtal hæmoglobin that can be accepted as abnormal. Similarly, it has not been clarified whether folic acid-levels can be measured in plasma or serum of normal persons not receiving folic acid therapy, a point of considerable importance in the recognition of folic acid-deficient states.

This number of the *British Medical Bulletin* is a valuable addition to the literature of hæmatology and should be read by all practising hæmatologists and by all clinicians, biochemists and students who have an interest in this ever-growing subject. A. A. SHARP

IDENTITY OF THE α-CHAINS OF ADULT AND FŒTAL HUMAN HÆMOGLOBINS

By J. A. HUNT

Medical Research Council Unit for Molecular Biology, Cavendish Laboratory, Cambridge

THE globins of human fœtal and adult hæmoglobins (hæmoglobins F and A) are known to differ in several ways[1a,b]. Hæmoglobin F contains more threonine, serine, methionine and tryptophan, and less proline, alanine, valine and histidine than hæmoglobin A; it also contains *iso*leucine not present in purified samples of hæmoglobin A[1b,2]. Hæmoglobin F is more stable to alkali than hæmoglobin A[1b], and in the erythrocyte hæmoglobin F has a greater affinity for oxygen[1a].

Hæmoglobin F was shown by Schroeder and Matsuda[3] to consist of two pairs of polypeptide chains with N-termini, valyl–leucine and glycine. Since Rhinesmith *et al.*[4] had shown that hæmoglobin A consists of two pairs of polypeptide chains with N-terminal sequences valyl–leucine and valyl–histidyl–leucine, called the α- and β-chains, it was suggested that the valyl–leucyl (α) chains of hæmoglobins A and F might be identical[3]. I have separated and compared these chains and find that, so far as can be judged by the methods used, they are indeed identical.

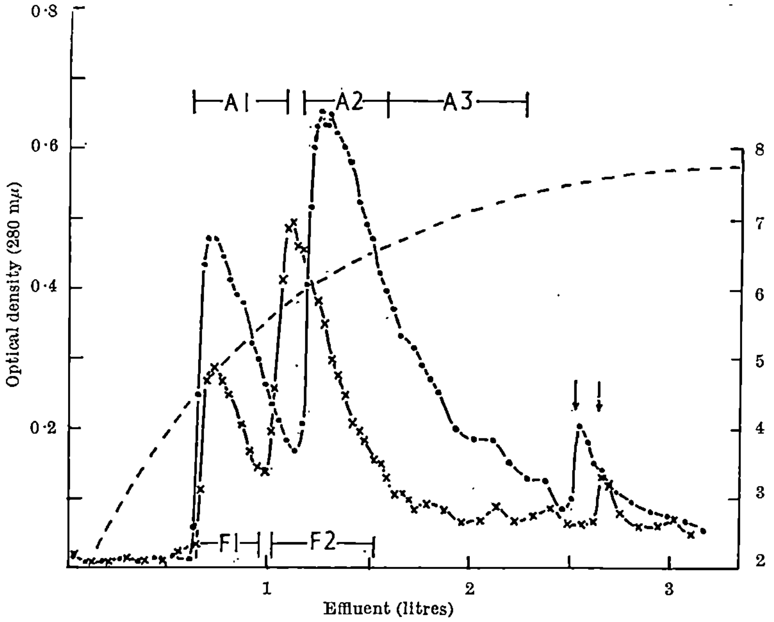

Fig. 1. Chromatograms of the globins A (700 mgm.) and F (300 mgm.) on '*IRC* 50' resin. The urea gradient was made by running 8 *M* urea at *p*H 1·9 into 1 litre of 2 *M* urea at *p*H 1·9. Because of the uncertainty of locating the exact starting point of the urea gradient, the positions of the peaks *A*1 and *F*1 have been adjusted slightly to coincide exactly. The two arrows mark the points at which 8 *M* urea at *p*H 1·9 was used to complete the elution. — · — · —, globin A; —×—×—, globin F; – – – –, urea

Hæmoglobin F was separated from cord-blood oxyhæmoglobin by chromatography on a column of 'Amberlite *IRC* 50'. Using a buffer (composition 3·9 gm. $NaH_2PO_4.2H_2O$ plus 2·66 gm. Na_2HPO_4 per litre), which had had its *p*H adjusted to 7·18 at 25° C. with 2 *N* potassium hydroxide, hæmoglobin F was eluted at the solvent front[5].

The constituent polypeptide chains of the globins, prepared by the method of Anson and Mirsky[6], were separated by gradient elution with urea at *p*H 1·9 on an 'Amberlite *IRC* 50' column[7]. The chromatograms of both globins show two peaks (Fig. 1), allowing fractions *A*1, *A*2 and *A*3 and *F*1 and *F*2 to be isolated. Fraction *A*3 contains less of fraction *A*1 as an impurity than fraction *A*2 and so was used in preference to *A*2.

After dialysis and lyophilization the fractions were subjected, without further denaturation, to tryptic digestion and chymotryptic digestion of the trypsin-resistant cores, in an autotitrator[8,9] using a ratio of enzyme to protein of about 1 : 100. The resulting peptides were separated by electrophoresis, followed by chromatography using Ingram's 'fingerprint' technique[8].

Fig. 2 shows 'fingerprints' of the tryptic digests of fractions *A*1 and *F*1 and the chymotryptic digests of their trypsin-resistant cores. The patterns are seen to be identical. Their identity was further confirmed by specific tests for arginine, histidine, tryptophan,

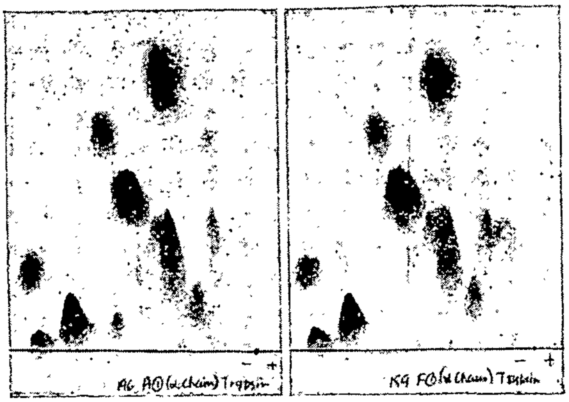

Fig. 2*a*. 'Fingerprints' of the tryptic digestions of fractions *A*1 and *F*1

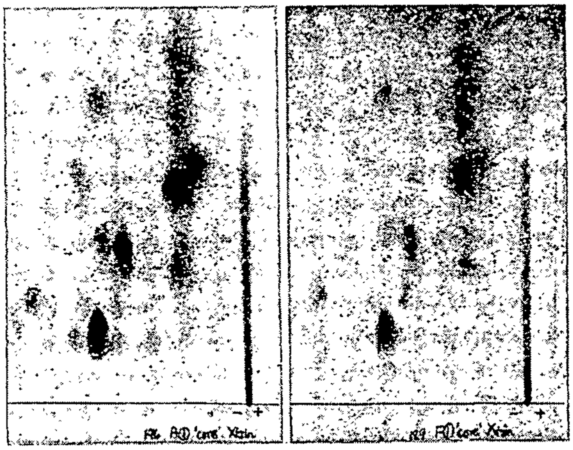

Fig. 2*b*. 'Fingerprints' of the chymotryptic digestions of the trypsin-resistant cores of fractions *A*1 and *F*1

tyrosine and sulphur[10], and by the identity of the ratios of tyrosine to tryptophan determined spectrophotometrically[11] (Table 1).

The N-terminal end-groups of the chains were determined allowing the fractions in 8 *M* urea to react with 1-fluor-2.4-dinitrobenzene at *p*H 8 and 38° C. (ref. 12). Table 2 shows that, on hydrolysis for an hour, dinitrophenyl valyl–leucine is the main product from *F*1 and dinitrophenyl glycine from *F*2. Since *F*1 is the same as *A*1, it must correspond to the α-chain of hæmoglobin A as defined by Rhinesmith *et al.*[4]. Hydrolyses for 15 min. of the dinitrophenylated fractions *A*1 and *A*3 showed that *A*1 contained mainly N-terminal valyl–leucine, confirming that it is the α-chain, while *A*3 contained virtually none. It was not possible to isolate di-dinitrophenyl valyl–histidyl–leucine. These results for *A*1 are in agreement with those of Ingram using the Edman degradation[13]. Leucine and *iso*leucine were separated from 22-hr. hydrolysates of fractions *F*1 and *F*2 on a one-dimensional chromatogram using 1 : 1 benzyl : butyl alcohol buffered at *p*H 8·4 (ref. 14). Measurements of the ninhydrin coloration eluted from the chromatogram showed that the ratio of *iso*leucine to leucine is less than 1 : 100 in *F*1 and approximately 1 : 6 in *F*2.

Table 1. Ratio of Tyrosine to Tryptophan of Fractions *A*1 and *F*1 determined by two different Methods

(*a*) Spectrophotometric determination, average of two values.
(*b*) Determined by specific stains on 'fingerprints'.

Fraction	(*a*) $\frac{\text{Tyrosine}}{\text{Tryptophan}}$	(*b*) No. of peptides containing: tyrosine	tryptophan
*A*1	3·0	3	1
*F*1	3·1	3	1

Table 2. Amounts of Dinitrophenyl Peptides and Amino-acids determined Spectrophotometrically, by Elution from a Paper Chromatogram, from 1 hr. Hydrolysates of the Dinitrophenylated *F*1 and *F*2 Fractions

val, valine or valyl; leu, leucine; gly, glycine

Fraction	Dinitrophenyl derivatives			
	O.D. 350 mμ	O.D. 360 mμ		$\frac{\text{val–leu + val}}{\text{val–leu + val + gly}}$
	val–leu	val	gly	
*F*1	0·71	0·12	0·02	0·98
*F*2	0·16	0·03	1·05	0·15

Fingerprints of the *F*2 and *A*3 fractions show many differences, which account for all the differences in the fingerprints of the whole globins A and F (Fig. 3).

Ingram has shown[13] that the amino-acid changes which characterize the mutant hæmoglobins S, C, Dβ and E occur in peptides of the β-chain of hæmoglobin A, whereas those of hæmoglobins I and Dα occur in the α-chain. In order to account for the genetic data of a family carrying the genes for hæmoglobins S and G, Schwartz *et al.*[15] proposed that there are two genes controlling the synthesis of hæmoglobin A; and the same proposal has been used by Smith and Torbet[16] in their study of Hopkins-2 hæmoglobin. Neither hæmoglobin G nor Hopkins-2 hæmoglobin has yet been characterized chemically, but it is possible that each of the two genes controls the synthesis of one of the chains of hæmoglobin A. If so, then the synthesis of each of the chains of hæmoglobin

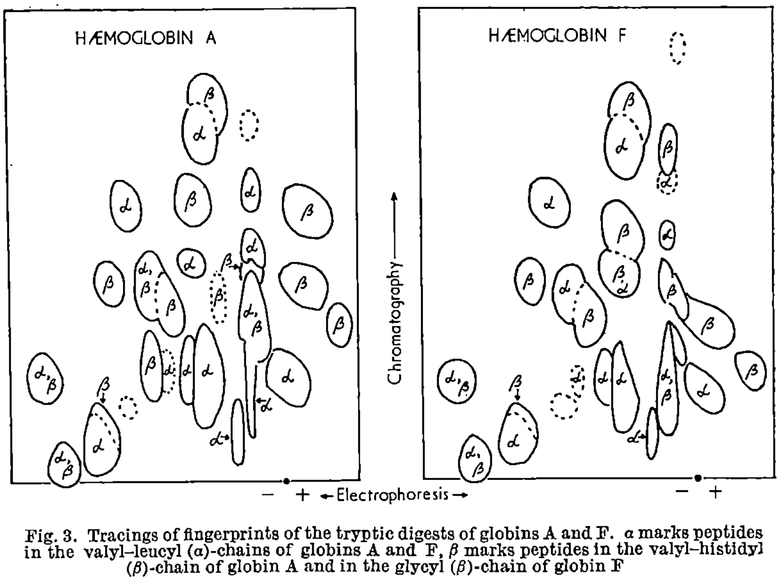

Fig. 3. Tracings of fingerprints of the tryptic digests of globins A and F. α marks peptides in the valyl–leucyl (α)-chains of globins A and F, β marks peptides in the valyl–histidyl (β)-chain of globin A and in the glycyl (β)-chain of globin F

F may also be controlled by a different gene, which would suggest that the α-chains of hæmoglobins A and F are controlled by the same gene. This possibility could be tested by studying the hæmoglobin F from individuals carrying hæmoglobins with α-chain mutations, such as[13] hæmoglobins I or Dα. If the same gene controls the synthesis of the α-chains of both the fœtal and adult forms, an abnormal fœtal hæmoglobin would be found. In individuals carrying mutations in the β-chain of adult hæmoglobin, the fœtal hæmoglobin is apparently normal, as is to be expected. On the other hand, one would predict the existence of abnormal fœtal hæmoglobins containing β-chain mutations associated with normal adult hæmoglobins[17]. Furthermore, only the gene controlling the β-chain would be affected in the switch-over from fœtal to adult hæmoglobin synthesis. The hæmoglobin system therefore offers opportunities for studying the control mechanism of gene action.

I thank Dr. Rayburn and the staff of the Cambridge Maternity Hospital for generously supplying the samples of cord blood, and Drs. Smith and Wilson (Ottawa) for allowing me to see the manuscript of their paper before publication. I am much indebted to Drs. S. Brenner and M. F. Perutz for their helpful discussions and encouragement.

I am grateful to the Medical Research Council for a Scholarship.

Note added in proof. I have just learnt that Drs. J. R. Vinograd and W. A. Schroeder, at the California Institute of Technology, have obtained similar results by a different method.

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DARK FIXATION OF CARBON DIOXIDE IN *KALANCHOE BLOSSFELDIANA* IN RELATION TO PHOTOPERIODISM

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PREVIOUS work[1] has shown that in *Kalanchoe blossfeldiana* var. Tom Thumb the capacity for dark fixation of carbon dioxide developed after previous exposure to a number of short days (> 13) and failed to develop either in long days or if the dark period was interrupted by an exposure of 10 min. to light given at midnight. Flower induction results only under the former conditions.

In a cycle of 8 hr. light and 16 hr. darkness the course of fixation of carbon dioxide during the dark period, using gas-analysis methods, showed that the rate of this process increases from zero at the beginning of the dark period and reaches a maximum after approximately 12 hr. (the critical dark period for flower induction), after which dark fixation rapidly falls off and gives place after 16 hr. to normal respiration, which is maintained at a nearly constant rate for a further 32 hr. of continuous darkness. This behaviour of induced plants of *K. blossfeldiana* var. Tom Thumb is in marked contrast with that of other succulent plants[2–4], in which the rate of uptake of carbon dioxide remains constant for several hours after darkening. For this reason the work here reported was undertaken to confirm previous findings.

In the course of this work it was found that there are marked varietal differences in the species *K. blossfeldiana*. The variety Feuer Blüte behaved in the normal 'Crassulacean' way in that dark fixation during the first 4 hr. of darkness was already maximal and slowly declined. Furthermore, in this variety the capacity to fix carbon dioxide in darkness was independent of the photoperiodic regime given, and indeed was greater in long than in short days.

The method consisted in exposing the tissue to carbon dioxide labelled with carbon-14 of known concentration and estimating the dark fixation by extracting the tissue at the end of the experiment with alcohol and estimating the radioactivity of the extract in the usual way.

The apparatus used was a 50-ml. conical flask with a centre well. The flask was sealed with a rubber serum cap and immersed in darkness in a water-bath at 20° C. It was possible to maintain a known concentration of unlabelled carbon dioxide by ventilation through two hypodermic needles inserted through the cap, one of which was attached to a gas cylinder. The tissue was contained in the annular space on wet filter paper to avoid injection. At various times during the dark period a known volume of labelled carbon dioxide was released from labelled sodium carbonate contained in the centre well by injecting excess of lactic acid through the cap from a hypodermic syringe ; immediately prior to this some air free of carbon dioxide was flushed through the flask and then the ventilating needles were removed. The exposure to labelled carbon dioxide was continued for 1 or 4 hr. periods. At the end of the period the tissue was immediately killed by adding boiling 80 per cent ethanol and complete extraction ensured by two further extractions. The extract was evaporated to small volume in a vacuum desiccator and cleared by centrifugation; the precipitate contained no carbon-14. Aliquots of the supernatant liquid were dried on duralumin counting plates and radioactivity estimated with an end-window counter. The disks, which contained little radioactivity after extraction, were dried and weighed. Results were calculated on the basis of infinite thinness and expressed as μl. carbon dioxide fixed per mgm. dry weight of extracted disk per hour.

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Plants used for the experiments were raised from cuttings of uninduced plants in growth chambers at 20° C. provided with fluorescent tubes giving an intensity of 1,000 ft. candles at the leaf surface. The short-day plants were given either 8 or 9 hr. and the long-day plants 16 hr. light periods. Preliminary experiments showed that it was necessary accurately to select leaves of the same age by using those from a known number of nodes below the apex.

Experiment with Variety Feuer Blüte

In this experiment, samples of 30 disks of 7 mm. diameter were taken from leaves of the upper ten nodes. The induction period was 97 days, by which time the short-day plants had produced numerous flower buds, while the long-day plants remained vegetative. Dark fixation was studied over four consecutive 4-hr. periods. During the previous light period the plants were exposed to full sunlight in a greenhouse. At the end of the light period, disks were immediately cut and placed in the flasks. The course of dark uptake over the first 16 hr. is shown in Table 1.

Table 1

	Interval of darkness during exposure to $^{14}CO_2$	μl. CO_2 fixed/mgm. dry wt./hr..
Short-day	0–4 hr.	0·55
	4–8 ,,	0·50
	8–12 ,,	0·53
	12–16 ,,	0·27
Long-day	0–4 hr.	0·85
	4–8 ,,	0·58
	8–12 ,,	0·64
	12–16 ,,	0·41

This shows that the maximal rate of dark fixation occurred in the first period, after which there was no marked change until 12 hr. darkness; it then declined. Dark fixation was actually greater in the long-day than in the short-day plants. In this respect the variety Feuer Blüte behaved as a normal succulent.

Experiments with Variety Tom Thumb

In a similar experiment the variety Tom Thumb was used. The short-day plants received a preliminary induction period of 75 days (9 hr. light, 15 hr. dark) in the growth chamber (1,000 f.c., 20° C.); visible flower buds appeared after 45 days. For each sample, 20 disks (7 mm. diam.) were used, taken from leaves of the upper eight nodes, and equally distributed among the treatments. Duplicate samples were taken from pairs of opposite leaves.

The long-day plants received 18 hr. light per day and were all vegetative at the time of sampling.

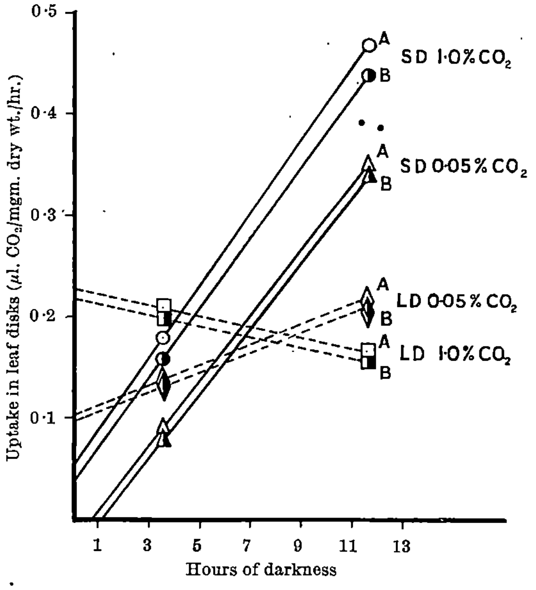

Fig. 1. Dark fixation of carbon dioxide by leaf disks of variety Tom Thumb; long-day and short-day plants. Half-shaded symbols denote duplicates

3 hr. after the beginning of the dark period one set of disks was exposed for 1 hr. to two concentrations of labelled carbon dioxide: 0·05 and 1·0 per cent, respectively. A second set was exposed after 11 hr. in darkness, at which time the dark uptake was expected to have attained a maximum. The results are shown in Fig. 1, in which results for duplicate samples in each treatment are given. In the short-day plants (S.D.) the rate of dark uptake is nearly proportional to the duration of darkness as the lines pass close to the origin. The long-day plants (L.D.) at both levels of carbon dioxide showed greater uptake than the short-day plants at the earlier period and maintained the level of uptake at similar rates in the later period. The unexpected results appear that, using disks, the long-day leaves showed appreciable dark uptake from the beginning of the dark period, whereas the short-day leaves again showed an increase from zero time.

As the earlier experiments of Gregory, Spear and Thimann[1] were performed with whole cuttings and the leaves were therefore entire, it seemed important to repeat the experiment using intact leaves. In other respects the experiments were similar to those already described.

The experiment was carried out on two occasions. In the first, 1 per cent carbon dioxide was used

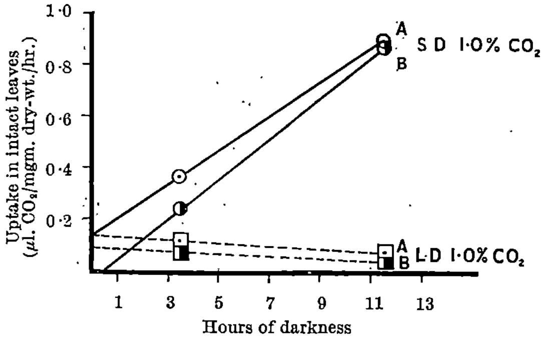

Fig. 2. Dark fixation of carbon dioxide by whole leaves of variety Tom Thumb. Half-shaded symbols denote duplicates

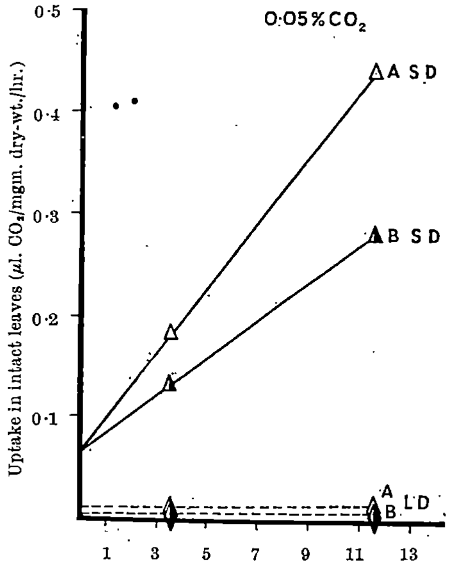

Fig. 3*A*. Dark fixation of carbon dioxide by whole leaves of variety Tom Thumb. Half-shaded symbols denote duplicates

with leaves from specific upper nodes for the earlier sample, and the opposite member of the leaf pairs from the same nodes for the later sample. Duplicate samples were taken from alternate nodes on the stem. The results are shown in Fig. 2. The rate of uptake of the intact long-day leaves was now less than that of short-day leaves, whereas the latter behaved as in the experiment using leaf disks.

Since the original experiments with whole cuttings were carried out in normal air, the second experiment employed two concentrations of carbon dioxide—1 and 0·05 per cent. Results are shown in Fig. 3 *A* and *B* and confirm previous findings.

Evidence has been presented from four experiments, all showing that the rate of dark uptake of carbon dioxide in the variety Tom Thumb after short-day induction increases through the dark period up to 12 hr., and begins at a very low level. In the long-day plants the uptake appears to be different, using disks as compared with entire leaves,

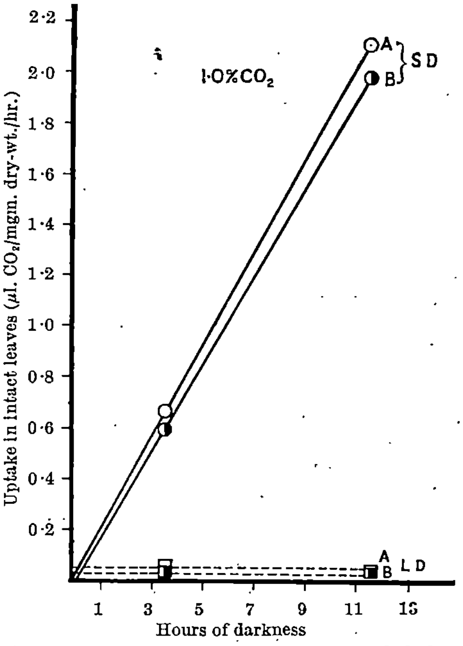

Fig. 3*B*. Dark fixation of carbon dioxide by whole leaves of variety Tom Thumb. Half-shaded symbols denote duplicates

the former showing much higher rates of fixation, which is maximal at the start of the dark period. The experiments with entire leaves confirm the findings of Gregory *et al.*, but the cause of the discrepancy between disks and entire leaves cannot at present be explained. The carbon dioxide which has direct access to the tissues through the cut edges of the disks is thus not subject to stomatal control; this may be important if stomatal behaviour in the dark varies between long- and short-day leaves as previously suggested[1].

One of us (G. Z.) acknowledges a postdoctoral research grant from the University of Illinois, Urbana, U.S.A.

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MODEL OXYGEN-CARRYING COMPOUNDS AND THE IRON-*BIS*-INDIGO COMPLEX

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ONE of the most challenging problems of biological chemistry is to explain adequately the ability of hæmoglobin to combine reversibly with molecular oxygen without undergoing oxidation. A closely related problem is the orientation of the oxygen molecule in oxyhæmoglobin. X-ray methods have not yet yielded this information, chiefly because of the complexity of the protein part of the molecule. Consequently, considerable interest attaches to those metal chelate complexes which can combine reversibly with oxygen to yield crystalline compounds. Many such compounds have been suggested as possible models for hæmoglobin; among these is a complex of iron and indigo which has been widely quoted as being capable of reversible combination with oxygen when in solution in pyridine. We have been investigating the chemistry of this complex, but before discussing our results, some relevant aspects of the problem will be summarized.

When hæmoglobin is oxygenated, the bivalent iron atom is not oxidized to the tervalent state but the effective magnetic moment decreases from 5·4 Bohr

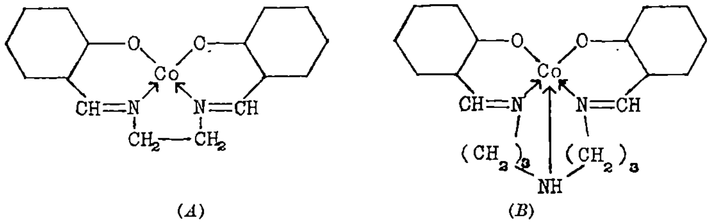

Fig. 1

magnetons (B.M.) to zero[1]. This indicates the formation of a spin-paired (inner orbital $3d^2 4s 4p^3$) octahedral complex. The behaviour of other metal complexes which combine with oxygen is relevant to the hæmoglobin problem. Thus, cobaltous *bis*-salicylaldehyde ethylene diimine (Fig 1, *A*) and chromous *bis*-acetylacetone[2] both absorb oxygen readily ; but only in the former case is the combination with oxygen reversible. Extensive investigations of oxygen-carrying cobalt complexes have been carried out by Calvin[3] and by Diehl[4] on many compounds derived from *A* and *B* ; also, Hearon[4] has studied the *bis*-histidinocobalt (II) complex. When oxygenated these paramagnetic cobalt (II) complexes decrease in susceptibility and, although the results are not easy to interpret, apparently spin-pairing occurs between the cobalt and oxygen atoms.

The aquopentamminocobalt (II) and aquotetraethylenepentamminocobalt (II) ions[5,6], and also[7] vitamin B_{12a}, have been reported to combine reversibly with oxygen under suitable conditions. The first of these is stated to show magnetic behaviour similar to that of the cobalt (II)–histidine compound. Vitamin B_{12a} is claimed to be the first cobalt (III) compound to combine reversibly with oxygen. The magnetic properties of these unusual compounds warrant investigation.

In oxyhæmoglobin the metal-porphyrin skeleton is small compared with the attached protein. Indeed, there is some evidence for believing that the hæm molecule is buried within the protein. For example, whereas the combining powers of ethyl *iso*cyanide, *iso*-propyl *iso*cyanide, and *t*-butyl *iso*cyanide with hæm are about the same, both hæmoglobin and myoglobin combine much more strongly with the smaller ethyl *iso*cyanide than with the larger *t*-butyl *iso*cyanide[8]. Crystallographic studies have shown that the iron atom is in a 'cleft' in the protein of myoglobin[9], and electron magnetic resonance investigations indicate that the normal to the hæm plane passes to the exterior of the molecule from the iron atom in the cleft[10]. Since the movement of an oxygen molecule to and from the iron atom in hæmoglobin is unlikely to be sterically hindered, Wang[11a] has suggested that the stability of oxyhæmoglobin compared with that of 'oxyhæm' is due to the presence around the iron atom of a region of low dielectric constant produced by hydrophobic groups of the protein. Then, he claims, the separation from the iron atom of the O_2^- ion, necessary for an oxidation process, cannot occur readily but neutral molecules have easy access. However, such a region of low dielectric constant can scarcely affect the relative stabilities of oxyhæmoglobin and oxyhæm ; and although it would produce a high potential barrier to the separation of ions, this is a kinetic rather than a thermodynamic difficulty. Other factors such as the effect of the ligands on the oxidation potentials of the iron atoms in the two compounds seem far more important. In this the imidazole group of the protein, which completes the co-ordination shell of the iron atom in hæmoglobin, must play an important part.

A knowledge of the orientation of the oxygen molecule with respect to the iron atom of the hæm would give valuable insight into the type of the bond between them. If the oxygen molecule is held parallel to the hæm plane, then the bond involved would presumably be similar to the multi-centre type found in ethylenic co-ordination compounds, for example $[PtCl_2.C_2H_4]_2$. (This structure is favoured by Griffith[11b] for theoretical reasons.) On the other hand, if it lies at right angles to the hæm plane, it is presumably held by a σ-bond end on to one atom together with possible dative π-bonding from the metal. A homonuclear molecule like oxygen would be expected to be held either at right angles to or parallel to the hæm plane (Fig. 2) : a heteronuclear molecule like nitric oxide would be expected to be at right angles to, or at a much smaller angle to, the hæm plane. Thus, several nitrosyls have been found to contain linear metal–N–O bonds[12] ; and one, $Co(NH_2CSSH)_2NO$, has been found[13] to have a metal–N–O bond angle of 135° with respect to the plane formed by the sulphur atoms of the thiocarbamate groups. However, Ingram[14] has reported, from preliminary electron magnetic resonance investigations, that the axis of the nitric oxide molecule in the nitric oxide hæmoglobin complex lies parallel to the hæm plane. One might have expected it to be at a small angle to this plane.

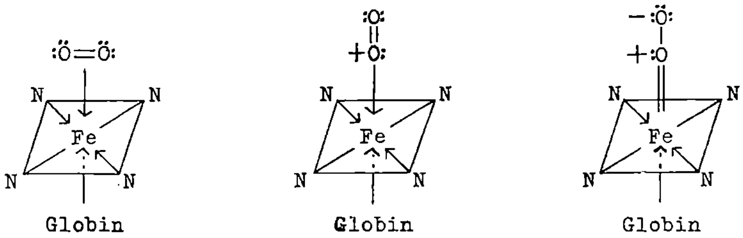

Fig. 2

Special interest attaches to the preparation of stable oxygen-carrying iron complexes as models. Thus, recently, the oxygen-carrying properties of the imidazole complexes of proto- and meso-hæm, and of ferrous dimethyl-glyoxime, have been studied by Corwin[15] and Williams[16] respectively. The imidazole complexes combine reversibly with oxygen in the solid state and when dissolved in pyridine : ferrous dimethylglyoxime show this property only in solution in the presence of bases, for example, imidazole ; in neither case have crystalline oxygenated compounds been reported.

Artificial oxygen carriers appear to be restricted to the compounds of cobalt and iron. (It is reported, however, that the μ-oxochlororhenate ion $(Re_2OCl_{10})^{4-}$ will combine reversibly with oxygen[18].) The cobalt compounds, except those derived from the parent compound *B*, suffer from the disadvantage, as model compounds, that the reversibly combined oxygen molecule is believed to form a bridge between the cobalt atoms in two adjacent molecules ; in effect,

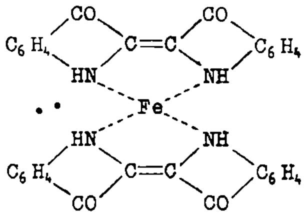

Fig. 3

one oxygen atom is reversibly held by each cobalt atom. The few oxygen-carrying chelates which contain iron have been reported to combine with one or two[16] oxygen molecules for each iron atom.

The iron-*bis*-indigo complex was first prepared by Kunz[7] and Kress[17], who claimed they had isolated the unoxygenated and oxygenated compounds in crystalline form. To these they gave the formulæ Fe(indigo)$_2$ and Fe(indigo)$_2$O$_2$ respectively. In addition, they found that the unoxygenated compound, which was prepared by treating an excess of iron pentacarbonyl with indigo suspended in pyridine, combined with nitric oxide and hydrogen cyanide but not with carbon monoxide. Because these workers could find no evidence for the evolution of hydrogen in the formation of the unoxygenated compound they assigned the formula shown in Fig. 3 to it and considered that the iron was united to the indigo by 'residual valencies', the apparent oxidation number of the iron atom being zero. This complex bears at least a superficial resemblance to hæmoglobin, and seemed likely to repay more detailed investigation.

The iron–indigo complex has been prepared by the method used by Kunz and its empirical formula confirmed. Its magnetic susceptibility has been measured by the Gouy method over the temperature-range 100–300° K. (Fig. 4). It behaves as a normal paramagnetic compound with $\theta = -25°$ K. and its magnetic moment is 5·4 B.M., corresponding to that of ferrous iron in a spin-free complex. For the molecule to be square planar, using $3d\ 4s4p^2$ hybridized orbitals, a spin-only moment of about 2·83 B.M. corresponding to 2 unpaired electrons would be expected[19]. The most likely structures, therefore, are a tetrahedral monomer or an octahedral polymer involving co-ordination to oxygen or nitrogen atoms of other molecules. The low solubility of the compound suggests the latter, but polymers might arise simply from hydrogen bonding. The susceptibilities of some impure specimens showed considerable dependence on field-strength. This is believed to be due to the absorption of traces of iron pentacarbonyl, which decompose into iron and carbon monoxide on drying. These impurities were eliminated by careful preparation. The compound is a yellow-brown crystalline solid which very rapidly becomes dark green upon exposure to oxygen. This colour change is not reversed if the solid is left under reduced pressure. If the increase in weight upon oxidation is taken to be due to the absorption of oxygen, between 2 and 3 oxygen atoms are absorbed for each iron atom. The magnetic susceptibility decreases upon oxidation and the magnetic moment calculated from measurements at room temperature is close to 4 B.M. If we assume that the iron atom is oxidized, the fall in moment may be due to spin–spin interaction in an oxygen-bridged ferric complex, since the spin-free moment of a ferric complex is 5·92 B.M. It could also arise from the formation of a ferric complex involving the use for bonding of one inner *d* orbital (for example, dsp^2 or dsp^3 hybridization) for which three unpaired electrons are expected (3·88 B.M.). Some susceptibility measurements have been made over a temperature-range with the oxidized compound, but these are difficult to interpret because ferromagnetic impurities are produced during oxidation.

The iron atom in iron pentacarbonyl is zero valent. To account for the production of a ferrous compound it must be assumed either that one of the indigo molecules is reduced during co-ordination with the iron atom or that hydrogen gas is evolved in the reaction. It has been confirmed that no hydrogen is evolved, and the action of methyl magnesium iodide on the unoxygenated compound has shown that it contains 4 active hydrogen atoms, that is, there is no net displacement of hydrogen atoms from the indigo molecules on co-ordination. Infra-red spectra of the unoxygenated compound show absorption bands which, from comparison with the spectra of indigo and indigo white, can be assigned to OH stretching vibrations. These disappear on oxidation, and new absorption bands appear in the carbonyl stretching region. The complex is decomposed by water and acids, but is soluble in hot, concentrated alkali. Its solubility in alkali suggests the presence of hydroxyl groups, as does its slight conductivity in pyridine. These observations indicate that one of the indigo molecules is present in a reduced form analogous to indigo white.

Kunz and Kress reported that when a solution of the complex in pyridine was exposed to oxygen the colour changed from red to green and one oxygen molecule was absorbed for each iron atom. If the pressure over the solution was reduced, or the green solution was allowed to stand under nitrogen, gas was evolved, the red colour being rapidly restored; more oxygen could then be absorbed. This process could be repeated several times until finally the compound was oxidized. This has been confirmed. However, their experiments were carried out in

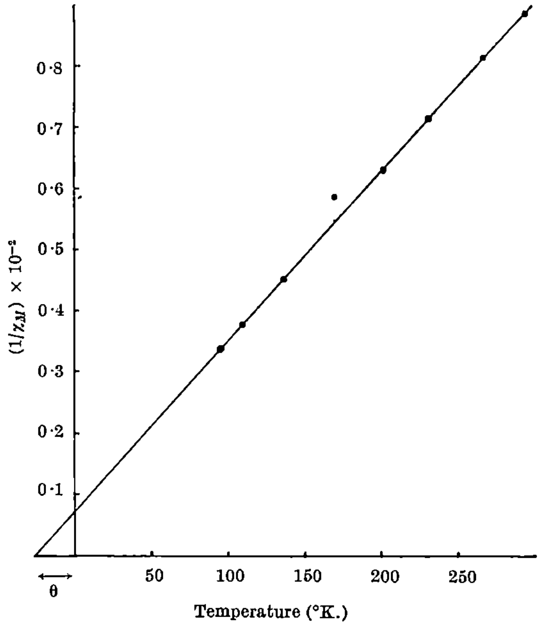

Fig. 4

solutions containing the excess of iron pentacarbonyl used in the preparation of the indigo complex, and the gas evolved could have been carbon monoxide produced as the residual pentacarbonyl reduced the green compound. In our experiments the gas evolved under reduced pressure from the oxygenated solution has been collected at atmospheric pressure by means of a Toepler pump and found to contain carbon monoxide together with all the oxygen previously absorbed. These experiments have been repeated in the absence of iron pentacarbonyl. Oxygen then produced the same colour change, and, although approximately 1 molecule of oxygen was rapidly taken up for each iron atom, much further oxidation soon occurred and the green solution became brown. The oxidation can be stopped at the green stage by pumping off the oxygen above the solution. When the green solution was allowed to stand under reduced pressure for several hours it became lighter in colour, but never the original red, and no oxygen could be detected in the small amount of gas evolved. Thus, the combination with oxygen is not reversible in the absence of iron pentacarbonyl.

When iron pentacarbonyl, or reducing agents such as hydrazine or sodium dithionite together with a little sodium hydroxide, were added to the green oxidized solution, the red colour was restored. It has been found that a ferrous salt, in pyridine, will give a green solution as soon as indigo is added; and the solution becomes red when reducing agents are added. On exposure to the air the solution becomes green, and these changes can be reversed until all the reducing agent is expended. The compound responsible for these changes has not been isolated, but it is probably identical with that prepared from iron pentacarbonyl.

The green oxygenated compound has been isolated from solution in pyridine, and from its analysis and infra-red spectrum is similar to the solid oxidation product. It also has a low magnetic moment, approximately 4 B.M., similar to that of the oxidized solid compound. It is not readily obtained because it is easily oxidized in pyridine. When it is dried under reduced pressure at varying temperatures it slowly loses weight, presumably because a slow reaction is occurring. Consequently, it is difficult to obtain an accurate analysis for the compound. The formula $\mathrm{Fe(indigo)_2O_2}$ assigned by the previous workers appears to have been based on an incomplete analysis. The substance is not suitable for X-ray measurements.

The unoxygenated compound reacts with nitric oxide or hydrogen cyanide. In solution in pyridine it was found to absorb 5 molecules of nitric oxide for each iron atom and in the process indigo was liberated. Since no protons were introduced in the reaction this established that no hydrogen atoms are removed from the indigo molecules on co-ordination. When hydrogen cyanide reacted with the unoxygenated compound dissolved in pyridine a yellow, crystalline compound was precipitated. Upon exposure to oxygen this compound rapidly became green. It is believed to have the formula $\mathrm{Fe(indigo)_2(CN)_2}$, but its investigation is not complete.

The co-ordination of an indigo molecule as a bidentate ligand can take place through 2 nitrogen atoms, 2 oxygen atoms, or a nitrogen and an oxygen atom. When two molecules are co-ordinated there are several possible formulæ, and if, in addition, one indigo molecule is assumed to be reduced, at least nine possible formulæ can be suggested. There can also be many different arrangements of the 4 hydrogen atoms in each molecule. A structure involving minimum re-arrangement, which is at least consistent with the infra-red spectra, is shown in Fig. 5; however, this would involve appreciable distortion of the bond angles. Structures in which the iron atom is co-ordinated to one oxygen and one nitrogen atom of the indigo residue are also feasible.

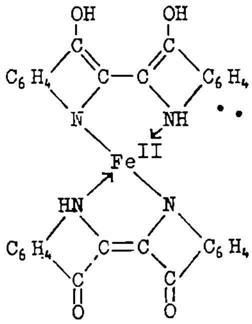

Fig. 5

In such a complicated molecule it is difficult to distinguish between the many possible formulæ without studying the infra-red spectra of many related compounds. We are now extending our studies to the indigo complexes of other metals in order to establish the structure of these compounds.

The oxidation of this complex, whether in the solid state or in solution, is undoubtedly a complicated process. Part of the reaction with oxygen must be oxidation of the iron atom to the ferric state, and part the oxidation of the chelate.

This work has shown that ferrous-*bis*-indigo is not capable of reversible combination with oxygen, and thus, as a model for hæmoglobin, is unsuccessful; and it illustrates the danger, in complicated molecules containing both metals and large organic ligands, of ascribing the reactions of the molecule to the metal atom without a complete knowledge of the structure of the molecule.

Our thanks are due to Dr. A. Earnshaw for making the magnetic susceptibility measurements; and to the Medical Research Council for a fellowship (L. F. L.).

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

Fusion Curve of Iron to 96,000 Atmospheres: Temperature of the Earth's Core

A NUMBER of arguments have been advanced[1] tending to show that the boundary of the Earth's core is molten iron, and the central part of the core is solid iron. If the Earth's core is composed of iron the solid phase of which near the melting point is the same as that at the surface, then a determination of the melting point of iron at about $1 \cdot 4 \times 10^6$ atmospheres (the pressure at the boundary between the mantle and the liquid core) would set a minimum temperature for this depth within the Earth.

No such pressures are available for static tests at the surface. For the present, it is necessary to be content with an extrapolation of the melting point to one or two million atmospheres. Recently, Simon and Gilvarry (see ref. 2) have published communications giving extrapolations of the melting point of iron to a few million atmospheres, using the results of experimental work on the initial slope of the fusion curve and certain theoretical deductions on its probable course[3].

Simon's and Gilvarry's extrapolations were extended over a pressure-range of six orders of magnitude in order to reach the pressure of the core boundary. We have now determined the melting point of iron experimentally to 96,000 atmospheres, so that the extrapolation is reduced to one order of magnitude in pressure. A brief summary of these results is presented here. A detailed account of the work on the melting point of iron, including a description of the structure of the sample and the method of measuring temperature and pressure, will appear elsewhere[4]. The apparatus used was the same as that used for the synthesis of diamond[5].

At a pressure of 96,000 atmospheres, the melting point of iron was found to be 1,740 ± 15° C. The error in pressure determination was estimated to be ±10 per cent. The fusion curve followed a smooth course over the entire pressure-range from 1 to 96,000 atm. with no indication of the existence of a triple point between γ, δ and liquid iron in the pressure-range covered. The lowest pressure at which a melting point was obtained was about 10,000 atm.

Simon's fusion equation (see ref. 3):

$$\frac{P}{a} = \left(\frac{T}{T_0}\right)^c - 1$$

fitted the experimental results with the constants $a = 75{,}000$ atm. and $c = 8$, and it was used to extrapolate the fusion curve to $1 \cdot 4 \times 10^6$ atm. pressure. In this equation, P is the pressure in atmospheres, T_0 the melting temperature in degrees absolute at the origin of the fusion curve at one atmosphere pressure, and T the melting temperature at pressure P. The extrapolated curve gave 2,340 ± 50° C. for the melting temperature at $1 \cdot 4 \times 10^6$ atm. Allowing for the effect of dissolved foreign atoms on the melting point and a drift of the extrapolation away from the true curve, the melting point at the boundary of the Earth's core should lie in the range 2,340 ± 200° C.

Simon (see ref. 2) used for a and c the values 150,000 atm. and 4 respectively, obtaining for the melting temperature of iron at the core boundary about 3,000° C. Gilvarry's[4] values for a and c were 347,000 atm. and $1 \cdot 9$, giving about 3,900° C. for the melting temperature at the core boundary.

During the course of the melting-point determinations, it was convenient to observe the β–γ transformation by the sharp change in slope of the electrical resistance–temperature curve which accompanies this transformation. At 76,000 atm. the transformation temperature had decreased to 705 ± 15° C. The initial slope of this curve was in the range $-8°$ to $-10°/1{,}000$ atm.

The parts of the phase diagram for iron determined from these experiments is illustrated in Fig. 1.

The iron used in these experiments was 99·94 weight per cent iron. The foreign atoms present included 0·0023 weight per cent oxygen, 0·002 carbon and 0·004 nitrogen. The largest single other impurity was 0·02 per cent nickel, the influence of which on the melting point was negligible.

I wish to thank Warren Moore and J. Schermerhorn of this Laboratory for the specimens of iron, Sherman

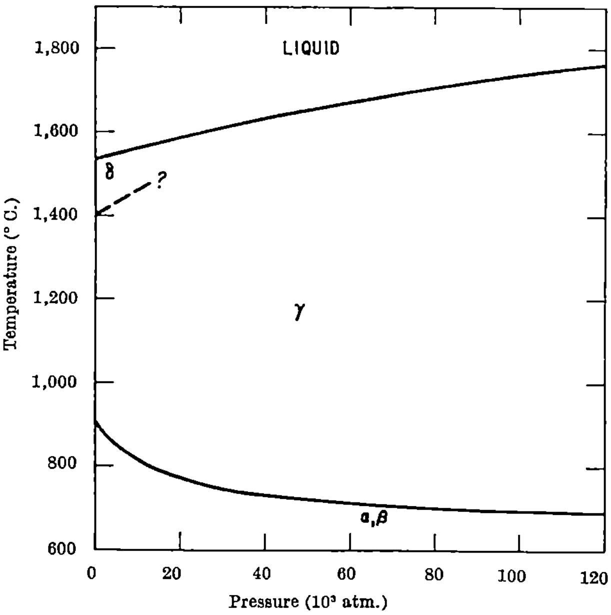

Fig. 1. Phase diagram for iron. The experimental results on the melting point were extended to 96,000 atm. and on the β–γ transition to 76,000 atm.

Reed and Wilson Weir for their excellent workmanship in constructing the test samples, and Roy E. Tuft for his valuable assistance in conducting the experiments.

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Sporadic *E*-Region Ionization, 'Spread F', and the Twinkling of Radio Stars

All these phenomena reveal the presence in the ionosphere of inhomogeneities in electron density of thickness some kilometres or less, the frequency of occurrence of which shows well-marked diurnal, seasonal, and geographical distributions, as well as correlation with geomagnetic activity. In the auroral zones they may be mainly due to ionization (in columns and sheets) produced by direct bombardment of the particles producing auroræ. However, auroræ occur rarely at moderate or low latitudes, where all these phenomena happen daily; in fact, at such latitudes the correlation of the latter with magnetic activity tends to be rather strongly negative.

A clue to the origin of these phenomena at non-auroral latitudes may lie in the fact that they appear to have one common feature: they occur most frequently or most intensely at times when the ionization of the relevant matrix region (*E* or *F*) is moving *upwards* under the influence of the electrodynamic forces associated with the ionospheric electric current systems responsible for the solar, lunar or disturbance geomagnetic variations. For example, equatorial sporadic *E*-region ionization is a maximum near noon, when the equatorial electrojet current is a maximum eastwards, and at 8–9 hr. lunar time[1], when the lunar electrojet has a similar maximum. Again, the occasional reductions of the equatorial day-time (eastward) electrojet which are associated with geomagnetic disturbance are accompanied by a corresponding reduction[2] in equatorial sporadic *E*-region ionization.

Some years ago it was suggested[1] that such *E*-region ionization was essentially due to vertical movements, and the phenomena associated with the drifting of an inhomogeneity in an otherwise uniformly ionized medium were afterwards examined[3]. In a region of negligible Hall conductivity (such as the *F*2-region) the effects are simple. A long cylinder of electron density $N + \Delta N$ aligned along the magnetic field H, and embedded in a medium of electron density N drifting perpendicularly to H with velocity V, drifts relatively to the matrix medium with the velocity:

$$v = -V\varepsilon/(2 + \varepsilon) \qquad (1)$$

where $\varepsilon = \Delta N/N$ and may have any numerical value. (It is easy to show also that a sphere of corresponding density drifts with the velocity $v = -V\varepsilon/(3 + \varepsilon)$.) In both cases the motion is simple; there is no distortion of the cylinder or sphere, which moves like a solid through the medium without interchange of ionization at its surface.

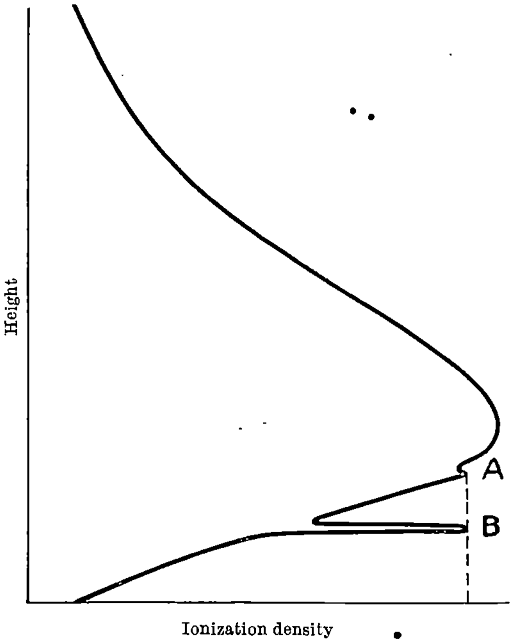

Fig. 1. Illustration of how a small positive perturbation of ionization density at *A* on the under surface of an upward drifting region becomes a large positive perturbation at *B* because it drifts upwards more slowly than the main body of the region

These results have been applied recently[4] to explain the occurrence of 'spread *F*', and the scintillation of radio stars. It has been shown that the ionization on the under-surface of the *F*-region is kinematically unstable when the region is drifting *upwards*. At such times a small irregularity (*A* in Fig. 1) drifts downwards relatively to the region and becomes a large irregularity (as at *B*) capable of producing the pronounced scattering responsible for scintillations and 'spread *F*'. It has been shown[4] that the magnitude of the inhomogeneities thus produced seems quantitatively adequate, while the times at which these phenomena should occur agree well with the known morphology of the occurrence.

At first sight it might appear that these simple considerations could also be applied directly to explain the formation of sporadic *E*-region ionization. Here, however, a difficulty appears. For the phenomenon depicted in Fig. 1 to occur it is essential that the life (relaxation-time) of the ionization in the irregularity be substantially longer than the time required to drift from *A* to *B*. This condition is adequately satisfied in the *F*-region, where the relaxation-time of the (night-time) ionization is about 2 hr.; it is certainly not satisfied in the (day-time) *E*-region, where the relaxation-time is only 3 or 4 min.

The difficulty disappears when the Hall conductivity of the *E*-region is taken into consideration. In such a medium it has been shown[3] that movement of a cylinder like a solid body is impossible. However, movement of a cylindrical perturbation of N is possible[5] in such a way that there is constant interchange of ionization between the cylinder and the medium at the surface of the cylinder. In other words, a cylindrical perturbation of ionization travels through the medium as a kinematic wave. For such a wave to be propagated from A to B and so produce a major inhomogeneity it is not necessary for the time of travel to be less than the relaxation-time of the medium ; it suffices if the wave travels a distance comparable with the radius of the cylinder in a time less than the relaxation-time. This condition is frequently satisfied in the E-region of the ionosphere for cylinders of less than about 1 km. diameter.

It can readily be shown that the velocity of the wave relative to that of the moving medium, and in the direction of the latter motion, is :

$$v = -\frac{V\varepsilon(2+\varepsilon)}{4(1+\varepsilon)\cos^2(\alpha-\beta)+\varepsilon^2} \qquad (2)$$

where tan α,β are ω_e/ν_e, ω_i/ν_i respectively, $\omega_{e,i}$ being the gyro frequencies and $\nu_{e,i}$ the collisional frequencies of the electrons and ions.

There is also a component of the wave velocity perpendicular to V, but in the ionosphere this cannot of itself lead to the generation of substantial inhomogeneities as it is mainly horizontal.

It will be noted that at heights of about 100 km., where cos $(\alpha-\beta)$ is about 1/20, $|v|$ may be up to five times $|V|$: the wave of inhomogeneity travels up to five times faster than the general drift of the medium. It seems almost certain that these waves are responsible for the production of equatorial sporadic E-region ionization, which appears at the times of solar, lunar and magnetic disturbances when the drift motion in the E-region is upwards and the wave motion consequently downwards for ε positive, thus leading to pronounced irregularities on the under-surface of the region. (For ε negative the wave motion is, of course, upwards, small deficiencies in N in the lower part of the region being transferred upwards to appear as substantial 'holes' near the ionization peak.) The recent discovery[6] that irregularities in sporadic E-region ionization at the magnetic equator are aligned horizontally along the geomagnetic field is also in accord with this finding. It also seems likely that these waves are responsible for much of the sporadic E-region ionization found in moderate latitudes. Their importance in auroral latitudes can be assessed only after further studies.

It is remarkable that the same basic fact, kinematic instability in the ionization gradient of a medium drifting across a magnetic field, should appear to be responsible for three geophysical phenomena, namely, scintillation of radio stars, spread F, and at least some forms of sporadic E-region ionization. However, no new concept is involved ; the relevant conclusions follow from the application of well-established electrodynamical principles to known ionospheric facts. The only approximation assumed is that the radius of the perturbation should be much less than the scale-height of the ionized region, a condition which seems safely satisfied in both regions E and F. Indeed, if these phenomena did not occur in the relevant parts of the ionosphere, it would seem to be necessary to explain why they were absent at the times and places where the ionization is known to have appropriate upward drift.

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April 1.

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A Type of Variation of the Signal Strength from 1958 δ2 (*Sputnik* 3)

This communication is based on observations of the *Sputnik* 3 signal strength carried out from the end of November 1958 at Kiruna Geophysical Observatory, Sweden (67·8° N., 20·4° E.). The 20·005 Mc./s. signals were received on a standard communications receiver (Collins 51 J–4) and recorded on a mV.-pen recorder with a full-scale deflexion time of approximately 1 sec. The receiver was connected to a fixed 'quad' 20 Mc./s. antenna with a very low directivity.

From the results (of about 200 recorded passings of *Sputnik* 3) it is possible to see that part of the sudden fluctuations of signal strength (superimposed on the regular Faraday pattern and rotational fading) seems to be connected with definite points of the orbit. Over a period of a few days they occur at an almost constant time, measured from the time of equatorial crossing, as the continuous change in time is very slow. These times agree well with the moments when the satellite is passing below or above its track from one or more revolutions before. Sudden drops of signal strength coincide with passages above earlier tracks, and enhancements with passages below. *Sputnik* 3 passes above the paths of the first to the fourth previous revolutions, and below those of the ninth to the thirteenth previous revolutions (900–1,400 min. before). These facts indicate that the satellite produces heavily ionized tracks of a very long lifetime. To test this hypothesis, 85 night-passages (with very good reception of satellite signal

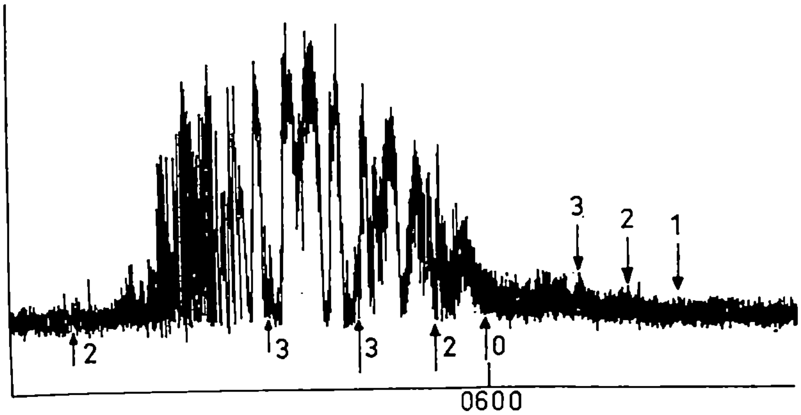

Fig. 1. A typical signal strength record (revolution number 3486) with arrows indicating predicted times of observed enhancements and drops and attributed weights w

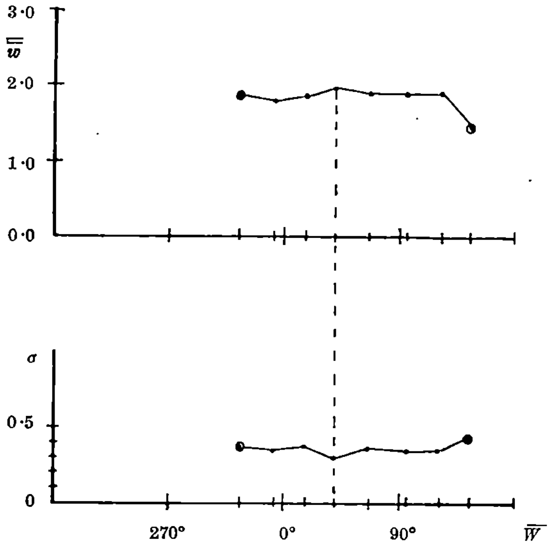

Fig. 2. The second mean weights, $\bar{\bar{w}}$, of the $\bar{w}$'s and the mean square deviations from $\bar{\bar{w}}$, σ, versus the mean longitude of equatorial crossings $\bar{W}$

and absence of interferences) during January 7–25, 1959, were investigated in the following way: the times at which one revolution crossed earlier ones were calculated approximately on the basis of the space-track bulletins[1]. If the predicted passage above a track coincided with a sudden decrease of signal strength, the 'crossing' was given a weight, w, from 1 to 3 (both time coincidence and the amplitude of the minimum were taken into account) and the weight $w = 0$ was attributed to the crossing if there was no decrease in signal strength. The corresponding procedure was used with passages below the tracks. A typical signal strength record with arrows indicating predicted times and attributed weights, w, is shown in Fig. 1. For every satellite passage the mean weight, $\bar{w}$, was calculated.

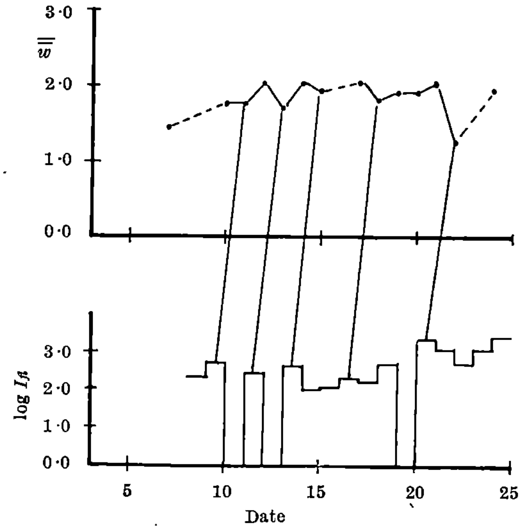

Fig. 3. The second mean weights, $\bar{\bar{w}}'$ (calculated for each night, irrespective of the longitude of equatorial crossings), and the logarithm of the High Altitude Observatory, Boulder, total flare activity index, I_{fl}, versus time

It is to be expected that $\bar{w}$ will depend on the geometrical configuration of the path of the satellite, with respect to the ionized track and the position of the observer, and also on the conditions in the ionosphere. The effect of geometrical configuration was investigated by grouping passages with respect to the longitude of equatorial crossing, W. For every group of passages the second mean weight, $\bar{\bar{w}}$, of the $\bar{w}$'s, was calculated, together with the mean square deviation from $\bar{\bar{w}}$. The result is plotted in Fig. 2. It can be seen that the highest value, $\bar{\bar{w}} = 1·95$, and the smallest dispersion of $\bar{w}$ is obtained for the group of passages with a longitude of equatorial crossing of about 44° W., that is, for passages nearest to Kiruna. It is evident that the time of crossing in a vertical plane and the time at which the radiation from the satellite traverses the earlier track should agree best for that group.

It is possible to see the influence of ionospheric conditions from seasonal changes of the second mean weight $\bar{\bar{w}}'$ calculated for each night (average of $\bar{w}$ for all passages during one night, irrespective of the longitude of equatorial crossings) (Fig. 3). The lower diagram of Fig. 3 represents the logarithm of the High Altitude Observatory, Boulder, total flare activity index, I_{fl}, versus time. Each decrease in $\bar{\bar{w}}'$ seems to be connected with an enhancement of solar activity, displaced in time about one day, as is to be expected.

The height of satellite 1958 δ 2 was always greater than 700 km. in the region of reception. The phenomenon is being studied in more detail.

I am greatly indebted to Dr. B. Hultqvist for valuable discussions. The work on which this communication is based has been supported by the European Office of Air Research and Development Command (Contract 61(514)–1314).

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March 17.

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[1] Distributed by the Space Track Control Center, L. G. Hanscom Field, Bedford, Mass.

The Twilight Radiation at 6708 A.

Recently, Delannoy and Weill[1] have reported a new atomic emission line in the spectrum of the twilight sky at Terre Adelie. The wave-length of the radiation is given as 6708 ± 1·5 A., and the authors suggest that the line may be the resonance line of lithium at 6707·8 A. The observation is confirmed, and the same identification proposed, by Gadsden and Salmon[2] (New Zealand and Antarctica). On the assumption that the identification is correct and that the lithium and sodium atoms are distributed in the same manner in the atmosphere, Barbier *et al.*[3] have computed the ratio of the concentration of lithium to sodium from the line intensities. They arrive at a ratio which agrees with the ratio found for the metals in meteorites.

The discovery of the new radiation was brought to my attention by Profs. Rosseland and Harang (Astrophysical Institute, University of Oslo) in January this year, and a search for the line was at once started at Aas, Norway (59° 40′ N., 10° 47′ E.). The instrument used was a grating spectrograph with a Bausch and Lomb plane grating, 102 mm. × 128 mm.,

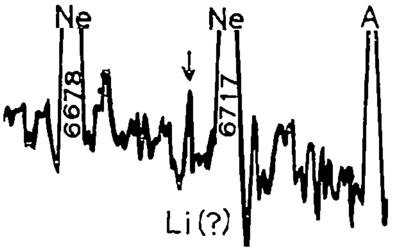

Fig. 1. Photometer tracing of a twilight spectrogram from January 23 (1735–50 M.E.T.). Lithium line indicated by arrow

600 lines/mm., blaze wave-length 1·6μ, and a camera objective from the Wray Optical Works, *f*/0·71, focal length 64 mm. The linear dispersions in the second and third orders are about 80 and 50 A./mm. respectively. (For a fuller description of the instrument see ref. 4.)

A series of twilight spectra, obtained on January 18 (Kodak 103 *aF* plate) in the third-order spectrum, showed a very sharp but faint line in the correct place. Later, the line was obtained in both the second- and the third-order spectra, showing that it really belongs to the red region.

Fig. 1 is a cutting of a photometer curve of one of the spectrograms, with a comparison spectrum superimposed (the neon lamp used contained traces of helium and argon). The line, supposed to be due to lithium, is indicated by an arrow. It is the only line in this region which extends across the spectrum and is therefore easily separable from the lines of similar intensity in the comparison spectrum (helium fourth order, neon and argon, not indicated in Fig. 1). Wave-length measurements from several spectra have given the mean value 6707·7 ± 0·5 A., which is very close to the value of the lithium resonance line. The proposed identification seems very plausible.

The line has been observed in both morning and evening twilight. Spectral series have been taken with the collimator of the spectrograph elevated 4·5° and 9·5°. The line appeared when the depression of the sun below the horizon was less than about 14·5° and 13° respectively. This is very nearly the same solar depression limits as those observed for the sodium *D*-line enhancement in twilight[5]. The lithium and sodium radiation thus probably originate from the same atmospheric level. (A difference of, say, 5 km. in the screening height of the lower atmosphere for the solar light responsible for the resonance excitation of the lithium and sodium atoms will result in a difference of about 3 km. in the heights of the two layers. This difference is certainly too small to be detectable except when the line intensities of the spectral series, and the azimuth and elevation angles of the collimator of the spectrograph, are measured with the utmost precision[6].)

Gadsden and Salmon[2] have reported a decrease of the lithium layer relative to the sodium layer of about 0·4 km. per day between August 13 and September 5, 1958. The results from Norway, collected from January 18 to February 20, 1959, indicate no such decrease of the lithium layer. In view of what is said parenthetically above it seems difficult without further evidence to accept the reported small decrease of the lithium layer, the more so as the authors themselves state that the Hallet spectra have not yet been available for precise measurements.

In a recent communication, Barber[7] suggests that the lithium atoms originate from atomic bombs, detonated in the central Pacific Ocean. His argument is based mainly on the observations of Gadsden and Salmon of the sudden (?) appearance of the lithium line on August 5 (a nuclear detonation occurred on August 1); the intensity ratio of the lithium and sodium lines, estimated to be about unity at Hallet; and the differential decrease of the lithium layer.

The latter observation seems doubtful. So does its explanation as an association of the lithium atoms with falling meteoritic dust or smoke particles from bomb explosions. It is not easy to understand why the free lithium atom, emitting the resonance radiation in the twilight, should not remain a free atmospheric constituent unaffected by dust and particles. A temporary or local high intensity of the line is, on the other hand, not a surprising observation in view of the great fluctuations of other airglow radiations[8]. The argument is therefore not completely convincing even if it is by no means improbable.

I am inclined to believe that more than one source are responsible for the metal content of the atmosphere. Evaporating meteorites, and to a small extent disintegration of atmospheric atoms by cosmic radiation, are probably permanent sources. Volcanic eruptions and nuclear bomb explosions may occasionally increase the concentration appreciably.

It has been stated that if meteorites are a major contributor, then other metals such as potassium and calcium should give observable radiations in the airglow. Calcium-ion radiation has been observed[9]. As for potassium, the detection of the resonance doublet at 7665 A. and 7699 A. is made extremely difficult by the great absorption of the oxygen (0,0) atmospheric band in that region. Some twilight spectrograms, taken with the grating spectrograph at Aas, have shown distinct increases of the 'background' radiation between the rotational absorption lines of the (0,0) band at the wave-lengths mentioned. I hesitate to state positively that this is the potassium doublet. Further observations are needed. Unfortunately a prolonged spell of bad weather has lately hindered observations.

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March 6.

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CRYSTALLOGRAPHY

Crystal Symmetry of Struvite (Guanite)

We have examined a small cluster of white crystals which were discovered in a can of Japanese crabmeat by Prof. H. E. Petch, McMaster University, Hamilton, Ontario. Spectrographic analysis showed

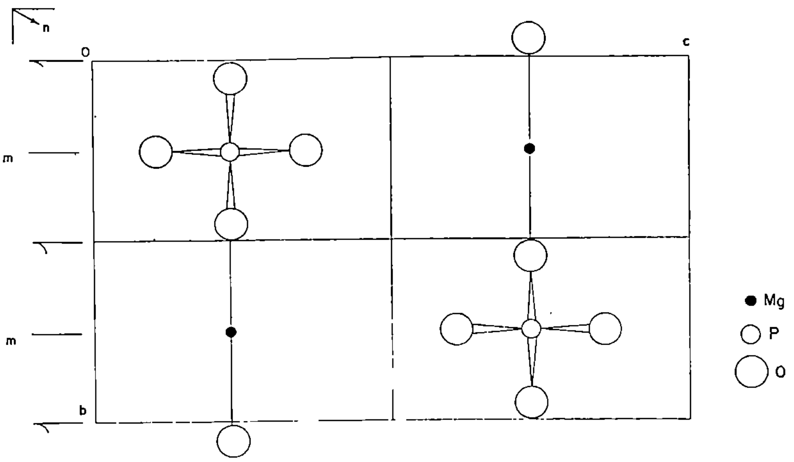

Fig. 1. Suggested partial structure of struvite projected on to the *bc* plane

that the crystals contained both phosphorus and magnesium, and the density, determined by flotation in a heavy liquid, was found to be 1·71 gm. cm.$^{-3}$. The crystals were insoluble in water. The unit cell and systematic absences of X-ray reflexions were determined from a small single crystal using a Buerger precession camera. They are: a_0 = 6·13 ± 0·02 A., b_0 = 6·92 ± 0·02 A., c_0 = 11·19 ± 0·02 A., $a_0 : b_0 : c_0$ = 0·883 : 1 : 1·616, *hkl* no absences, *hk*0 no absences, 0*kl* $k+l = 2n+1$ absent, *h*0*l* no absences, *h*00 no absences, 0*k*0 $k = 2n+1$ absent, 00*l* $l = 2n+1$ absent. The space group is $Pnm2_1$ and the a_0 axis has pseudo-hexagonal symmetry.

The crystal has been identified as struvite (or guanite), which Dana[1] describes with a chemical composition $Mg(NH_4)PO_4.6H_2O$, point group *mm*2 and axial ratios 0·8827 : 1 : 1·6102. The corresponding unit cell obtained from X-ray measurements is stated to be a_0 = 6·09 kX., b_0 = 6·97 kX., c_0 = 11·18 kX., which is in reasonable agreement with the cell obtained by us. The space group given by Dana[1] is *Pmc*2, which is not consistent with the systematic absences reported above. Instead, when our observations are combined with the morphological symmetry, they indicate unambiguously the non-centrosymmetrical space group $Pnm2_1$. Finally, Mellor[2] reports that struvite has a density of 1·715 gm. cm.$^{-3}$ and has a very low solubility in water.

With this information, some of the features of the atomic structure of struvite may be predicted. The density calculated on the basis of a cell content $Mg_2(NH_4)_2(PO_4)_2.12H_2O$ is 1·72 gm. cm.$^{-3}$, which is very close to the observed value. Since, in the space-group $Pnm2_1$, the general positions are four-fold and the special positions on mirror planes are two-fold, it follows that the magnesium and phosphorus atoms and the (NH_4) group must all lie on mirror planes perpendicular to the b_0-axis. It is expected that each phosphorus atom will be at the centre of an oxygen tetrahedron so that four of the oxygen atoms will lie on two sets of special positions and four more oxygen atoms will be in general positions approximately 1·3 A. from the mirror planes in the *y*-direction. A possible arrangement of these atoms is shown in Fig. 1 projected on the *bc*-plane. If the magnesium atom has the same *x*-co-ordinate as the oxygen atom in the general position, then there will be a chain of atoms, O—O—Mg—O, in the *y*-direction with normal bond-lengths O—O = 2·8 A. and Mg—O = 2·05 A. and with a repeat length 6·9 A.; this is the observed length of the b_0 axis. If we are correct in supposing that the oxygen tetrahedra have the orientation shown in Fig. 1, then a suitable position for the NH_4 group would be directly above the phosphorus atom. The nitrogen atom would then be tetrahedrally bonded to four oxygen atoms such that $O—NH_4$ = 2·5 A. It is not possible to place the twelve remaining oxygen atoms with certainty, but it is reasonable to expect that the magnesium atom will be octahedrally co-ordinated by oxygen atoms or water molecules as in $MgHPO_3.6H_2O$ (Corbridge[3]).

Some support for this structure is provided by a Patterson projection on the *bc* plane given in Fig. 2. This was computed with rough intensities obtained from a precession picture, using reflexions obtained with molybdenum *K*α radiation with $\sin \theta/\lambda \leqslant 0·55$. It is thought that peak *A* is produced by Mg—P vectors and peak *B* by Mg—O and P—O vectors. The remaining peaks cannot be accounted for without speculating on the other oxygen positions. No detailed comparison of F_0 and F_c was made but it was observed that the proposed atomic positions are consistent with large observed intensities from the planes 040, 004 and 048.

Struvite has been found previously in canned fish: Palache[4] reports the discovery of this substance in canned shrimp and Ayres[5] describes its occurrence in canned lobster. Both writers suggest that the presence of ammonia indicates that the crystals are produced by bacterial fermentation. Other remarkable occurrences of struvite are mentioned by Dana[1]: it was first found in Nature in a bed of peat under an old church in Hamburg, Germany, and was found in bat guano from the Skipton Caves, Victoria, Australia, and with newberyite in the tooth of a mammoth from Quartz Creek, Dawson, Yukon. In all these instances it appears that the compound was the result of decomposition of organic matter.

It should be noted that Mellor[2] states that large crystals of struvite can be readily prepared in the

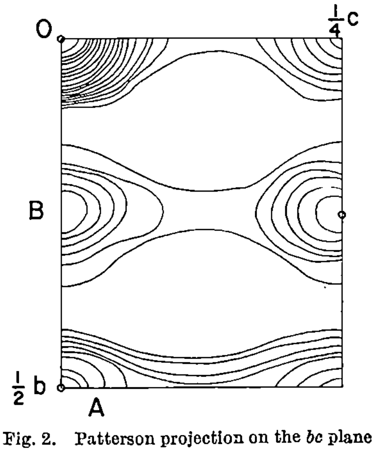

Fig. 2. Patterson projection on the *bc* plane

laboratory. Since the crystal lacks a centre of symmetry, is piezoelectric and has a good (001) cleavage perpendicular to the polar axis, it is likely that thin plates could be prepared for the examination of possible ferroelectric effects.

We do not plan further work on this compound.

We are grateful to Mrs. B. Murray for her help in obtaining the X-ray photographs.

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Absolute Measurement of the Intensity of the (111) Reflexion for Diamond

Atomic scattering factors of carbon atoms in the valence state, as computed by McWeeney[1], are in close agreement with the values obtained on the basis of measurements on diamond[2]. An exception occurs only in the f_C-value of (111), which was found to be 3·299, while McWeeney's theoretical value is close to 3·100.

To clear up this discrepancy, a careful re-determination of the absolute intensity of the (111) reflexion of diamond has been made. To avoid extinction effects, the measurements were carried out on a fine and pure diamond powder of particle size about 0·5μ. Particles of this size might still show some extinction. However, this influence on the intensity should be small and not exceed 1 per cent. The discrepancy is much larger.

The intensity was measured by two different techniques, surface reflexion and transmission. A Geiger proportional counter was used ('Norelco') and crystal monochromatized radiation. To avoid λ/2 in the monochromatized beam, voltages not higher than 14 kV. were applied to generate the copper *K*-radiation.

Table 1 contains the results.

Table 1

Method	Operation of X-ray tube		$1/8\ F_{111}$
	kV.	m.amp.	
Reflexion	14	20	2·211
,,	10	20	2·212
,,	14	20	2·222
,,	12	20	2·037
,,	14	18	2·166
,,	14	18	2·168
,,	14	18	2·104
Transmission	14	18	2·295
,,	14	18	2·206
,,	14	18	2·256

The mean value of these measurements was taken in two different ways, with and without weighting the accuracy of the single measurements. The weighted mean is $1/8\ F_{111} = 2{\cdot}20 \pm 0{\cdot}07$, $f_C = 3{\cdot}11 \pm 0{\cdot}10$, whereas the unweighted mean is $1/8\ F_{111} = 2{\cdot}18_8 \pm 0{\cdot}07$, $f_C = 3{\cdot}09 \pm 0{\cdot}10$. Both these values agree with the figure calculated by McWeeney within the limit of error.

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METALLURGY

Structure of Scale on Plain Carbon Steels

The classical picture of high-temperature scales on plain carbon steels as determined by Pfeil[1] shows a three-layered structure. An outer layer of hæmatite, Fe_2O_3, a middle one of magnetite, Fe_3O_4, and an inner one of wüstite, FeO, next to the parent metal is the normal composition of this layered structure in a scale that is continuous with the parent metal. (For practical and historical reasons, wüstite is normally given as the stoichiometric FeO when in fact it is more accurately described as $Fe_{1-Y}O$, where *Y* is the concentration of vacancies.) Similarly, Paidassi[2], in his recent work on the kinetics of oxidation of pure irons between 700° and 1,250° C., found that the three-layered structure is present on continuous scales. However, 15 min. was the minimim oxidizing time for the lower-temperature scales that he reported.

It is known that the simple layered structures of plain carbon steel scales are modified in practice by the production of pores and blisters. After a short initial period of oxidation, these defects occur rather readily. Furthermore, in the laboratory the production of continuous scales by extensive oxidation requires elaborate surface preparation including high-temperature anneals in hydrogen to produce a clean surface prior to the oxidation experiment.

It has been assumed generally that the structure of the thin scales on the products of the modern continuous rod and strip mills conformed to the classical picture of scale structure. However, during the microscopic examination of the scales of these products, unusual types of structure were observed. Fig. 1 illustrates one type of structure first noticed on samples of wire rod. It was considered rather unusual at the time. However, in the examination of narrow hot strip samples extensive regions of this type of structure were observed (Fig. 2). It has been given the description of a 'sandwich' structure. There is almost no evidence of blistering and it is essentially a continuous scale with the parent metal.

The innermost layer in contact with the parent metal is magnetite. The middle layer is wüstite and the next layer is again magnetite. In some instances a thin outer layer of hæmatite is also observed. This unusual innermost layer of magnetite is similar in appearance to the outer primary magnetite layer when examined under the optical microscope. Its micro-hardness is also of the same order as the primary magnetite layer. When etched it appears as a single phase with sharp boundaries, and in no way resembles the dark-etching decomposed wüstite

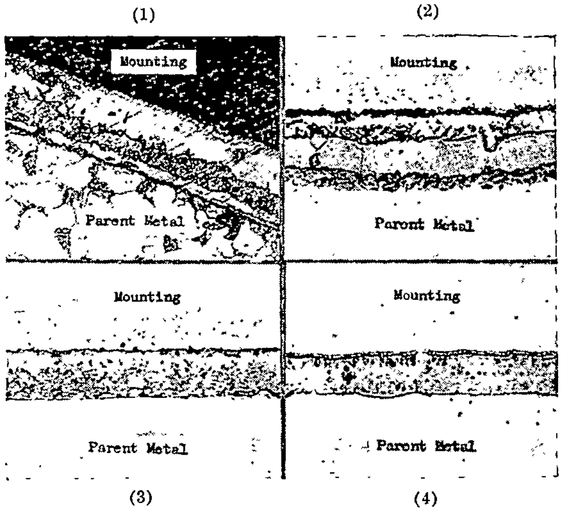

Fig. 1 (× 250) Figs. 2–4 (× 500)

illustrated in Fig. 3. This dark phase is apparently composed of fine magnetite and ferrite particles originating from the breakdown of wüstite. The boundary between the dark-etching material and the primary magnetite layer is rather indefinite when etched with a solution of citric and hydrochloric acid in methyl alcohol. The micro-hardness of this decomposed layer is similar to that of the primary magnetite.

In other structures observed on samples of wide strip mild steel, the entire scale appears to be composed of a single phase of primary magnetite. The scale towards the edges of the strip also has a thin hematite layer on top of the magnetite layer (Fig. 4).

The non-classical appearance of these structures must, of course, be associated with their origin in high-speed strip and rod mills and their thermal history after the last shaping operation, coiling and removing from the finishing line.

Whereas the decomposed wüstite phase (Fig. 3) can be readily explained by existing knowledge it is rather difficult to visualize the mechanism of the formation of the inner magnetite layer next to the parent metal. Collongues, Sifferlen and Chaudron[3] have shown that although wüstite is unstable below 570° C., its decomposition is dependent on the cooling-rate of the oxide below that temperature. They found that the kinetics of the isothermal transformation of wüstite can be expressed as an *S*-curve with the nose of the curve giving the maximum rate of transformation occurring at 480° C. Fischer, Hoffman and Shimada[4] and Fischer and Hoffman[5] have shown metallographically the breakdown of wüstite in bulk at temperatures below 570° C.

The presence of an inner layer of magnetite in the sandwich structure would be explained if it were assumed that it was originally wüstite which had decomposed below 570° C. The high concentration of oxygen next to the parent metal could be produced by either a mechanism of reverse diffusion of iron atoms back to the parent metal or by the internal oxidation of the scale at the scale–metal interface.

In those structures that show no wüstite it must then be assumed that the mechanism which produced an inner layer of magnetite was able to progress to the point where the entire wüstite layer was transformed.

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Fatigue Properties of Ternary Aluminium–Zinc–Magnesium Alloys

EXPERIMENTAL work[1] has suggested that the poor fatigue properties of age-hardened aluminium alloys are due largely to the metastable nature of the dispersed precipitate. Cyclic stressing causes deformation to become progressively more localized and the precipitate in these regions may become unstable. This leads to softening which, in turn, causes a further concentration of deformation in these regions and the whole process becomes catastrophic. The mechanism by which softening occurs is uncertain, but it is thought to be associated with dislocation movements in the localized regions. It thus seems that the fatigue properties of these alloys would be improved if the stability of the dispersed precipitate could be increased or if a reduction in the mobility of dislocations in the highly stressed regions could be effected. This communication describes some initial experiments in which the second possibility is being investigated.

The mobility of dislocations may be reduced by interaction with solute atoms. Thus, in an age-hardening alloy, it would seem desirable to have present solute atoms which play no part in the ageing process and are free to participate in such interactions. A recent study of ageing phenomena in a number of ternary aluminium–zinc–magnesium alloys[2] has suggested that, when the magnesium : zinc ratio exceeds a certain value, excess magnesium atoms are present which are not required in the ageing process. This conclusion becomes more significant when it is recalled that yield-point phenomena have been observed[3] in binary aluminium–magnesium alloys, indicating that interactions can occur between magnesium atoms and dislocations. These observations suggested that a study of the effect of composition on the fatigue properties of a range of ternary aluminium–zinc–magnesium alloys might provide some interesting results.

Six alloys were selected in which the magnesium : zinc ratio was widely varied but for which the same heat-treatment cycle of solution treatment for 1½ hr. at 460° C., cold water quench, and ageing for 16 hr. at 125° C. gave approximately the same value of ultimate tensile strength[4]. By keeping these variables constant the fatigue properties could be compared with some standard of reference. Details of the actual compositions and tensile properties are given in Table 1.

Rotating cantilever fatigue specimens of 0·300 in. test diameter were prepared from forged and heat-treated bars. Standard machining techniques were used and the final surfaces of the test sections

Table 1. Alloy Compositions and Tensile Properties

Alloy	Magnesium (Mg)	Zinc (Zn)	Mg/Zn	0·1 per cent proof stress (P.S.) lb./sq. in.	Ultimate tensile strength (U.T.S.) lb./sq. in.	0·1 per cent (P.S./U.T.S.)	Elongation (per cent)
B	1·05	8·3	0·13	44,000	55,200	0·80	14·4
C	2·0	5·8	0·35	47,600	58,300	0·80	15·5
D	3·0	5·1	0·59	44,900	59,000	0·76	17·7
E	4·0	4·5	0·89	31,000	54,300	0·57	30·0
F	5·0	4·1	1·22	31,800	53,200	0·60	27·7
G	6·0	3·7	1·62	47,000	56,000	0·84	15·5

were prepared with a tungsten carbide-tipped tool.

Complete *S*—*N* curves for each alloy were not determined, but the results clearly showed that the fatigue properties vary greatly with composition (Fig. 1). Highest fatigue properties were obtained with alloys *E*, *F* and *G*, which had the largest magnesium : zinc ratios. Of these three alloys, *F* had much the best properties, and it should be noted that the magnesium : zinc ratio in this case was between those of alloys *E* and *G*. Somewhat lower properties were obtained with *C* and *D*, which had zinc and magnesium contents similar to the current commercial high-strength alloys. Alloy *B* had the lowest fatigue strength and, in view of the high zinc content, this may be due partly to grain boundary brittleness.

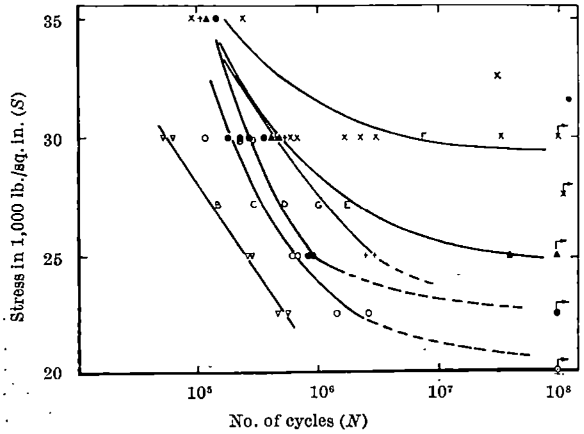

Fig. 1. Partial *S*–*N* curves for the alloys

The relationship of fatigue properties to tensile properties is also significant, since it has been proposed[5] that, in aluminium alloys, good fatigue strength is associated with low ratios of 0·1 per cent proof stress to ultimate tensile strength. Alloys *E* and *F* had 0·1 per cent proof stress values well below the values for the other alloys. However, this can only partly account for the higher fatigue properties of these two alloys since, although they had similar ratios of 0·1 per cent proof stress : ultimate tensile strength, the fatigue strength of *F* was notably better.

It thus seems likely that the high fatigue strength achieved with alloy *F* is primarily associated with a critical zinc : magnesium ratio. Whether, in fact, this is due to the interaction of excess magnesium atoms with dislocations cannot be stated. Further experimental work is in hand and this will be reported later.

Thanks are due to the Chief Scientist, Australian Defence Scientific Service, Department of Supply, for permission to publish this communication, and to Messrs. J. Y. Mann and J. M. Finney, who carried out the fatigue tests.

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CHEMISTRY

Electron Affinity of Oxygen

In recent years there has been considerable argument concerning the electron affinity of oxygen[1,2], and it is the purpose of this communication to direct attention to recent developments in this field resulting from work carried out with a Lozier ionization chamber apparatus in the Department of Electrical Engineering, University of Liverpool. A full account will be published elsewhere in due course.

For many years, following the work of Lozier[3], the value of the electron affinity of oxygen was accepted as 2·2 eV., and this value has recently been reinforced by the work of Metlay and Kimball[4], who employed a flame spectroscopy method. However, work by Branscomb and Smith[5], using the elegant photo-detachment method, yielded a value of 1·45 ± 0·15 eV., later amended[6] to 1·465 ± 0·005 eV., which was incompatible with the earlier work. The situation has been further confused by the work of Schüler and Bingel[7], who obtained values of 0·98 eV. and 1·05 eV. using a spectroscopic method. Hagstrum[8] attempted to re-interpret electron impact experiments in terms of the photo-detachment value, with some success except in the case of the dissociative attachment process in oxygen. However, values in the region of 2·0 eV. have been so consistently obtained by electron impact work in oxygen as to suggest that the discrepancy is not due to any of the more obvious experimental errors which have been suggested by various workers since 1955. In a recent paper[9] reasons have been advanced for believing that these errors do not appear, at least in the work carried out at Liverpool. So it may fairly be said that, so far as electron impact experiments are concerned, the situation has remained one of unresolved confusion.

Branscomb[1] has attempted to resolve the situation, and has suggested possible errors in the work of Metlay and Kimball, and of Schüler and Bingel. However, in my opinion, the electron impact situation has still remained unclarified.

At Liverpool, measurements of the electron affinity of oxygen have been carried out in carbon monoxide, carbon dioxide and oxygen, and have yielded values of 1·75 ± 0·1, 2·05 ± 0·2 and 2·0 ± 0·1 eV., respectively. The only apparent differences between the conditions of measurement lies in the initial kinetic energy of the ions at the electron energy at which they are first formed. These energies are, respectively, 0, 2·7, 1·6 eV. These measurements, and almost all earlier measurements, have been carried out using an electron beam which is not entirely monoenergetic, and calculations have shown that, due to the technique employed in obtaining the appearance potential of ions of a given kinetic energy, the spread in the energy of the electrons becomes of considerable importance where the initial kinetic energy of the ions is appreciable. Correcting for this error, the values for the electron affinity of oxygen obtained in carbon monoxide, carbon dioxide and oxygen become respectively 1·6 ± 0·2, 1·65 ± 0·3 and 1·5 ± 0·2 eV., all of which are compatible with the photo-detachment values. This error would be expected to occur in all electron impact experiments which do not employ an effective electron energy filter, and some supporting evidence has apparently recently accrued from the work of Randolph and Geballe[10], in which great care is taken to eliminate any error due to electron energy spread, and in which a value of 1·52 ± 0·1 eV. has been obtained. However, the appearance potential for O^- ions reported by these workers seems to be remarkably low. It would then appear that values of E (O) obtained by the electron impact method are subject to a subtle experimental error which makes most values obtained in this way incorrect unless the kinetic energy of the ions involved can be measured and allowance made. There no longer seems any reason to doubt the value of 1·465 eV., obtained by the photo-detachment method.

I wish to thank Prof. J. D. Craggs for his help and guidance, and Dr. R. Thorburn for many helpful discussions. I also wish to acknowledge receipt of a maintenance grant from the Department of Scientific and Industrial Research.

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A Spectrophotometric Method for the Determination of Chlorine

Rapid determination of low concentrations of chlorine is very important in analysis. The estimation of this element in the air (in industrial towns and factories) as well as its quantitative estimation in the laboratory work require rapid and precise methods.

In this communication a spectrophotometric method for the estimation of low concentrations of free chlorine is described. The chlorine was dissolved in an organic liquid and the absorption spectrum of the solution was examined in the ultra-violet region. This spectrum is most probably due to the formation of some complex compounds of chlorine. The absorption maximum of chlorine dissolved in carbon tetrachloride has a wave-length of about 335 mμ (Fig. 1) and its height is proportional to the concentration of chlorine. A standard curve (Fig. 2) was established with a Zeiss universal spectrophotometer. The concentration of the chlorine in the standard solution of the carbon tetrachloride was determined by potentiometric titration, and by dilution of this standard solution other samples were prepared. The sensitivity of the spectrophotometric method is about 2×10^{-5} M, that is, about 1 μgm. chlorine/ml. The other methods for the determination of chlorine (estimation as chloride ion or colorimetric analysis) are too slow and rather unreliable[1,2].

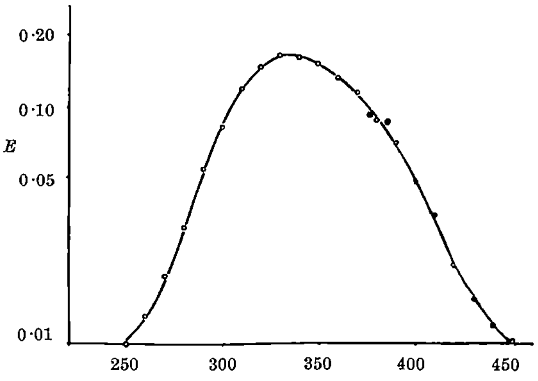

Fig. 1

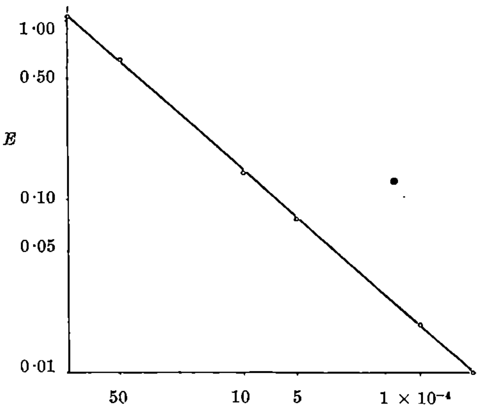

Fig. 2

In the same way, chlorine dissolved in other organic liquids such as chloroform, trichlorethylene, tetrachlorethylene, acetone, etc., can be determined. However, these analyses are less sensitive than those with carbon tetrachloride.

The method was used for the direct measurement of the chlorine content of carbon tetrachloride and chloroform irradiated with X-rays. It is also useful for the estimation of low concentrations of chlorine in the air and other gases, and for the chemical analysis of free chlorine.

I wish to thank Dr. M. Horák, of the Chemical Institute of the Czechoslovak Academy of Sciences, for the measurement of the ultra-violet spectrum, and Mrs. Šulcová and Mr. Hruška, of the Institute of Nuclear Research, for their help in the experimental work.

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Polymorphic Transitions in Anhydrous Sodium Sulphate

The heat capacity of anhydrous sodium sulphate has been measured recently in a water calorimeter by Kreidl and Simon[1], who observed only one high-temperature transition, at about 238° C. However, there are two known polymorphic transitions between room temperature and 300° C.: (1) the transformation of the stable low-temperature form V to the intermediate form III and (2) transformation of III to the stable high-temperature form I. The heat of transition observed by Kreidl and Simon was nearly equal to the sum of the heats of the two known transitions. They concluded that in the presence of water, the transition V ⟶ I occurs directly and reversibly, and supported this conclusion with X-ray diffraction data. More recently, Bird[2] has reported an irreversible transformation, V ⟶ I, upon heating sodium sulphate in the absence of water. This occurred at a considerably lower temperature of about 176° C., and is based on comparison of high-temperature X-ray diffraction patterns.

We have now subjected anhydrous sodium sulphate (reagent grade) to differential thermal analysis in the absence of water, using a high-sensitivity apparatus[3]. The rate of heating was maintained constant at 12 deg. $min.^{-1}$ over the entire range 25–350° C.; however, it was not possible to control the rate of cooling so closely. The curves are shown in Fig. 1. It should be noted that the reaction peak temperatures are by no means absolute, but are constant only for a given set of experimental conditions.

Only one transition peak was observed in the differential thermal analysis curves, beginning around 235° C. on heating. The transition is completely reversible, even though the sample was free of water. The areas under the peaks, which are proportional to the heats of the reaction involved, are of the same order of magnitude for both the endothermic (heating) and exothermic (cooling) peaks.

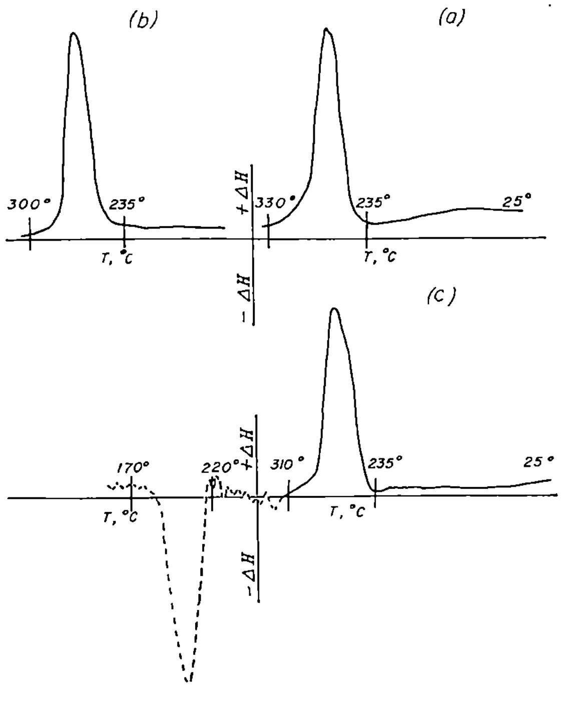

Fig. 1. Differential thermal analysis curves of anhydrous sodium sulphate between 25° and 350° C. (*a*) Heating curve, (*b*) heating curve obtained after cooling the sample (*a*) to 25° C.; (*c*) heating (solid line) and cooling (dotted line) curves

We thank Mrs. M. P. Lewis for her kind assistance in operating the differential thermal analysis apparatus.

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BIOCHEMISTRY and PHYSIOLOGY

Proton Transfer and Supercontraction in Actomyosin

It has been previously reported that the synaeresis of actomyosin gels with adenosine triphosphate is accompanied by changes in the X-ray diffraction pattern indicating that some part of the actin–myosin complex undergoes supercontraction[1]. The recent observation by Goodall[2] that one or more protons at each active site are involved in the production of tension in the myofibril is in line with my experiments, which suggest that the supercontraction of myosin (or actomyosin), long postulated as the fundamental basis of muscle contraction[3], might also be due primarily to some specific transfer of protons.

Earlier investigation showed that actomyosin apparently supercontracted on acidification, but the drastic nature of the treatment (2 per cent acetic acid) did not preclude the possibility of artefacts from partial hydrolysis. More recently, however, I have succeeded in preparing films of actomyosin from very weakly acid dispersions of the gel, and from neutral films weakly acidified and washed at neutrality, that show the characteristic reflexion at 4·65 A. on the meridian of the X-ray diffraction diagram. In every case, the hydrogen ion, rather than any anion combination of chloride, phosphate and acetate, appears to be responsible for the change.

The transformation into the supercontracted state, as judged by this test, becomes detectable below *p*H 6·0. Thixotropic gels of actomyosin allowed to stand for 48 hr. at *p*H 5·0, for example, form insoluble precipitates indistinguishable from those formed on addition of adenosine triphosphate at neutrality. When actomyosin from fish dorsal muscle is dried from a slightly acidified dispersion of the gel, the X-ray diffraction diagram is always characterized by a marked cross-β pattern, and at *p*H values in the region of 5·0 the meridional reflexion at 4·65 A. predominates over the 5·1 A. α-reflexion. Again, the X-ray diffraction diagrams of similarly prepared actomyosin gels dried at neutrality show a progressive increase in the cross-β pattern with increasing acidification and time of treatment. Immersion of the films at *p*H 5·0 for 48 hr., for example, followed by washing at neutrality, drying and mounting, results in the appearance of a clear supercontracted component after orientation by stretching (Fig. 1).

The ease with which these small changes of *p*H bring about the X-ray signs of supercontraction in actomyosin suggests that the system is extremely sensitive to protons. It might be argued that although adenosine triphosphate induces supercontraction at

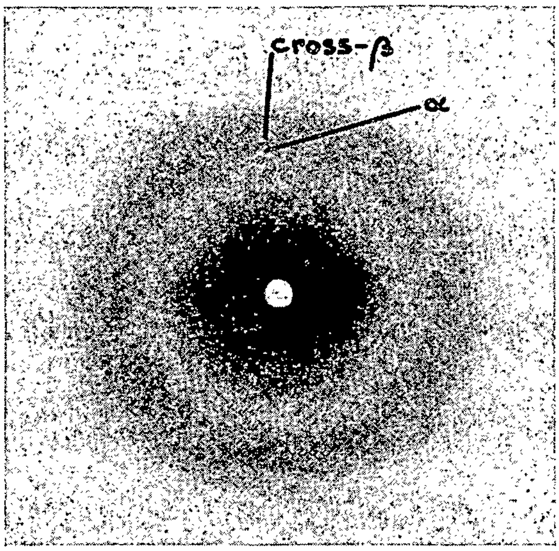

Fig. 1. X-ray diagram of a film of actomyosin dried at neutrality, treated for 48 hr. at pH 5, washed to neutrality, re-dried and oriented by stretching

neutrality, the attendant drop in pH during splitting[4] is in fact the cause of an artefact. It seems more likely, however, that the transference of protons during the splitting of adenosine triphosphate is the fundamental event itself, and that experiments involving protons alone are simply another expression of the fact that local migration of protons to some part of the actin–myosin complex causes collapse of specific polypeptide chains. Overall shortening of the complex will then take place according to the arrangement of the sites where the adenosine triphosphate is split.

I thank Prof. W. T. Astbury for his encouragement of this work, Dr. G. N. Graham for assistance in the preparation of actomyosin, and Mr. A. Millard for the photographic reproduction of Fig. 1. The work, which is aided by a grant from the Muscular Dystrophy Associations of America, Inc., will be described in detail in due course.

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Effect of Fatty Acid Mixtures on the Rice Stylet Nematode (*Tylenchorhynchus martini* Fielding, 1956)

In the course of other experiments, the metabolic fatty acids produced by *Clostridium butyricum* Prazmowski were shown to be active against *Tylenchorhynchus martini* Fielding, 1956. Fatty acids in aqueous solutions at those concentrations extracted from artificial culture filtrates proved highly effective in inactivating *T. martini*[1].

In the present work all possible combinations of the extracted acids—butyric, propionic, acetic and formic—were prepared at concentrations of 10^{-2}, 10^{-3} and 10^{-4} M in distilled water. Equal quantities of each acid in each combination were prepared at the various concentrations. Twenty active nematodes were submerged in each acid solution at each concentration until all the nematodes were quiescent. If the nematodes remained quiescent for 15 min. after they had been removed from the acid solutions into water they were considered to be inactivated. The pH of the acid solutions was determined.

Although nematode response was variable, it is evident from the results presented in Fig. 1 that the combination of butyric and propionic acids was more effective at 10^{-3} and 10^{-4} M than either butyric or propionic acid alone. Other results (not presented in Fig. 1) show that any combination containing 2, 3 or 4 of the above-mentioned acids was more effective than any one acid alone at the same molar concentration. Effectiveness of the acid mixtures was related to combined molecular weights. Thus, butyric and propionic acid mixtures were more effective than propionic and acetic acid mixtures. Relative effectiveness of the individual acids was dependent on their molecular weights and decreased in the order of butyric, propionic, acetic and formic. The pH-range of all solutions was between 3·3 and 4·4.

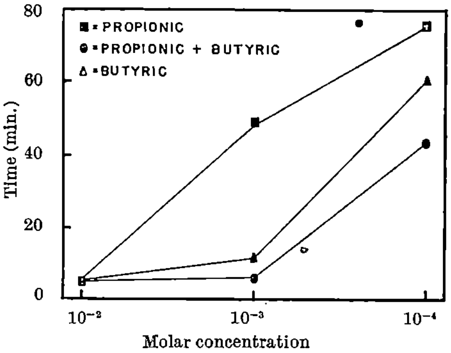

Fig. 1. Time in minutes required for inactivation of *T. martini* in water solutions of butyric and propionic acids and a mixture of the two acids at three different molar concentrations

Other experimental procedures thus far have failed to elucidate the mechanism of the effects of mixtures and single acids on this nematode.

Thanks are due to Dr. John P. Hollis at Louisiana State University for his constructive advice during this study.

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Free Radicals from Chlorpromazine

The report has been made recently of the isolation in urine of a metabolite of chlorpromazine which was designated as a free radical from its electron spin resonance[1]. Absorption data revealed no distinct characteristics in the ultra-violet and visible ranges. The same compound was formed also by photo-oxidation with ultra-violet light. The oxidation-level of the free radical was thought to be intermediate between chlorpromazine and its sulphoxide, and, as a result, a provisional formula was suggested involving the heterocyclic sulphur.

As a result of oxidation of chlorpromazine with hydrogen peroxide and peroxidase, Cavanaugh[2] obtained a red reaction product which had an absorption maximum at 527 mμ as well as an identical absorption in the ultra-violet as the sulphoxide. It was concluded from kinetic data that this substance was a precursor of the sulphoxide.

Finally, Dushinsky and Lishkova[3] obtained a red reaction product from the oxidation of chlorpromazine and ceric sulphate, which was considered to be a free radical from titrimetric evidence.

We have found chlorpromazine easily oxidized by ferric salts[4] in dilute acidic media, resulting in a red reaction product. The reaction appears to be specific for it does not occur with cupric, mercuric, zinc, molybdate, cobaltic, manganic or chromic ions. Nor does it occur when the iron is complexed as in ferricyanide. There is also some specificity on the part of chlorpromazine, for the sulphoxide does not give the reaction. However, if concentrated sulphuric acid is added, the sulphoxide does react, as, of course, does chlorpromazine[5]. This may be useful in differentiating the two compounds.

The red reaction product formed has absorption maxima at 530 and 255 mμ and a broad band in the range 270–275 mμ. This differentiates it from the substance investigated by Forrest *et al.*[1]. The absorption in the 270 mμ range is characteristic of the sulphoxide[6], and one would be led to agree with the proposal that the red-coloured reaction product is a precursor of the sulphoxide. However, this cannot account for the fact that the sulphoxide itself forms a red reaction product with concentrated sulphuric acid which has an absorption maximum at 530 mμ.

The stoichiometry of the reaction may be determined by assuming that better than 90 per cent of coloured reaction product is formed in concentrated sulphuric acid. This has been found true for other phenothiazine derivatives[7], and it can be used as a standard to determine the amount of coloured reaction product formed in the reaction with ferric ion. This, together with the determination of ferrous ion formed using different concentrations of reactants (Table 1), indicates that two molecules of ferric ion are necessary to oxidize chlorpromazine. This stoichiometry would favour a quinoid formulation rather than a free radical for the coloured reaction product. The ease with which chlorpromazine reacts with ferric ion suggests that the pharmacological activity of chlorpromazine might involve the cytochrome system. Evidence in this direction has been recorded in the literature[8].

Table 1

(C.R.P.) formed	(Fe^{2+}) formed	$(Fe^{2+})/(C.R.P.)$
0·0069	0·015	2·2
0·0083	0·015	1·8
0·014	0·032	2·3
0·015	0·034	2·3
0·018	0·043	2·4
0·022	0·048	2·2
0·023	0·052	2·3
0·023	0·041	1·8
0·025	0·054	2·3
		Average = 2·1

C.R.P., coloured reaction product.

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Isolation of an Activator for Phospholipase *D*

WHILE working on the purification of phospholipase *D* for use in connexion with other studies on phospholipids[1] we observed that incubation with the enzyme released choline from commercial soy bean lecithin, but not from synthetic L-α-dipalmitoyl lecithin or carefully purified lecithins from egg, yeast and soy beans. The apparent discrepancy has been resolved by isolation of an activating phospholipid from commercial soy bean lecithin preparations.

The incubations were conducted in 2 ml. of acetate buffer, *p*H 5·8, containing 0·05 molar calcium. The requirement for the latter ion as reported by Davidson *et al.*[2] was not affected by the presence of the activator. Enzymatic activity was determined by assaying the amount of choline liberated[3].

The enzyme was purified by centrifugation at 20,000*g* of an aqueous extract of cabbage acetone powder. The supernatant solution was lyophilized, redissolved in one-tenth the original volume of water and precipitated between 40 and 66 per cent of saturation with ammonium sulphate.

This procedure increased the specific activity eighty-fold. The total enzymatic activity recovered from the precipitation was approximately twice that of the original extract, apparently because of the loss of an inhibitor which has been previously reported[4,5]. Cabbage acetone powder provides an exceptionally stable source of the enzyme; a preparation stored at −10° C. has yielded active extracts for more than two years.

The activator was first separated from substrate by chromatography on a silicic acid column. However, this separation could be more rapidly effected by a precipitation procedure in which 100 ml. of ethanol was added to a solution of 5 gm. of commercial lecithin in 25 ml. of ether. The residue from evaporation of the mother liquor was reprecipitated from 10 ml. of ether.

Chromatography of 200 μgm. aliquots on silicic acid impregnated paper in system *A* of Marinetti and Stotz[6] showed that lecithin was absent from the combined precipitates but that a slightly more polar spot, similar in R_F to phosphatidyl inositol, was present

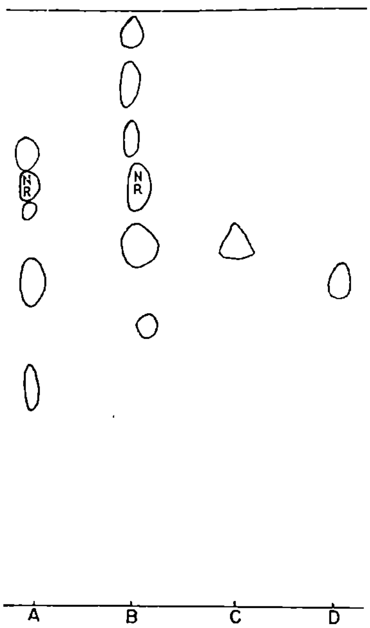

Fig. 1. Chromatograms of soy bean phospholipids on paper impregnated with silicic acid. Ascending solvent was di-*iso*butyl ketone/acetic acid/water, 40 : 30 : 7. *A*, ethanol-insoluble precipitate containing activator; *B*, ethanol-soluble fraction; *C*, lecithin substrate; *D*, activator after purification by column chromatography. All spots were visualized by immersion in dilute rhodamine *G*. Spots labelled *NR* also reacted with ninhydrin

as a major component. Almost none of this latter substance was present in the mother liquor (Fig. 1).

Separate incubations of precipitate, mother liquor residue and a reconstituted mixture of the two components in amounts equivalent to a total of 20 mgm. of starting material released 0·02, 0·17 and 0·52 μmole of choline respectively. The latter figure was in good agreement with the 0·59 μmole released from 20 mgm. of starting material.

Purified lecithin for use as a substrate in further experiments was obtained by chromatography of the residue from evaporation of the mother liquor on alumina and silicic acid according to the procedures of Hanahan and Jayko[7] and Lea, Rhodes and Stoll[8].

The activating factor was purified from the crude alcohol precipitates by chromatography on silicic acid. Fractions of the eluates from these columns were examined by paper chromatography and by incubation with 10 mgm. amounts of pure lecithin and phospholipase *D*. The results indicated that the enhancement of the hydrolysis of lecithin was associated with the component that was slightly less mobile than lecithin on the impregnated papers of Marinetti and Stotz. The chromatographic properties of this substance were indistinguishable from those of a phosphatidyl inositol prepared from peas[9] which was also found to activate the hydrolysis of lecithin by phospholipase *D*.

In the final isolation procedure columns of Mallinckrodt silicic acid containing 30 gm. adsorbent/gm. of lipid were eluted with chloroform–methanol 9 : 1 v/v until the yellow colour moving down the semi-translucent column was well separated from an opaque band which remained at the top. The latter was isolated by extrusion of the column, and a slurry of the extruded silicic acid in chloroform–methanol was poured into a smaller column. This material was eluted with chloroform–methanol 9 : 2 v/v until no weighable residue remained from the evaporation of 2 ml. of eluate. Chromatographically pure material could then be recovered by elution of the column with chloroform–methanol 7 : 3.

Inositol, but no choline or amines reacting with ninhydrin, could be identified chromatographically[10] in the water-soluble products from hydrolysis of this fraction for 48 hr. in 6 *N* hydrochloric acid. This, together with the chromatographic properties, indicates that the activator is the phosphatidyl inositol characterized by Okuhara and Nakayama[11] and by Hanahan and Olley[12].

The effects of the purified activator on the hydrolysis of lecithin are summarized in Table 1.

Table 1. Effect of Increasing Amounts of Activator on Total Choline released in 15 min. from an Incubation Mixture containing 5 mgm. Lecithin and 0·12 mgm. Enzyme/ml.

Mgm. activator/ml. of incubation mixture	Choline released (μmoles)
0·0	0·12
0·07	0·38
0·25	0·82
0·50	1·77
1·0	2·05
2·5	2·09

Another enzyme, phospholipase *B* of *Penicillium notatum*, has been shown by Dawson[13] to hydrolyse the ester bonds of lecithin only if phosphatidyl inositol or certain other lipid activators are present. It is possible that similar mechanisms are involved in the activation of the two enzymes, although the role of the inositide is still obscure. The two systems appear to differ markedly in their response to calcium ion, which is obligatory for phospholipase *D* activity, but which has been reported[13] to inhibit the activation of phospholipase *B*, perhaps by interfering with the formation of a complex between lecithin and phosphatidyl inositol.

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Prevention of Freezing Damage to Living Cells by Dimethyl Sulphoxide

Polge, Smith and Parkes[1] first reported the protective action of glycerol against the adverse effects on spermatozoa of freezing and thawing. Lovelock[2] found that the protective action of glycerol was shared with a number of other neutral solutes of low molecular weight, including methanol, acetamide and glyceryl monoacetate. Using the extent of hæmolysis of red blood-cells as a measure of damage

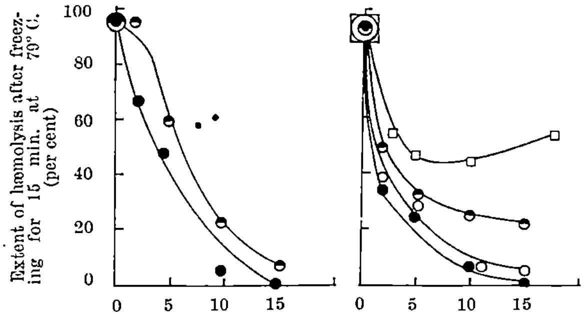

Fig. 1. The protective action of glycerol and of dimethyl sulphoxide against the hæmolysis of human (left) and bovine (right) red blood-cells by freezing and thawing. (◓, After prior exposure to glycerol for 30 sec.; ●, after prior exposure to dimethyl sulphoxide for 30 sec.; □, after prior exposure to glycerol for 2 hr.; ○, after prior exposure to dimethyl sulphoxide for 2 hr.)

by freezing, it was concluded that the principal protective action of the neutral solutes was a simple consequence of their ability to prevent the excessive concentration of electrolytes and other substances that otherwise occurs on freezing. The protective property is limited to substances that are in themselves not toxic, have a low molecular weight, a high solubility in aqueous electrolyte solutions and an ability to permeate living cells. The number of solutes capable of fulfilling these conditions is small, and so far glycerol most closely approaches the ideal protective agent. Some cells, however, are impermeable to glycerol, for example, bovine red blood cells, and with these glycerol is of little use in their preservation by cold storage. An alternative solute with a greater permeability to living cells is dimethyl sulphoxide. This communication reports the protective action of dimethyl sulphoxide against freezing damage to human and bovine red blood cells and to bull spermatozoa.

Freshly drawn human or bovine red blood cells were suspended in 0·16 *M* sodium chloride solution containing 0·1 per cent glucose. The cell suspensions were cooled to 0° C. and to them was added either glycerol or dimethyl sulphoxide to provide final concentrations of 2, 5, 10 and 15 per cent by weight. After allowing intervals of between 10 sec. and 2 hr. for the solute to penetrate the cells, they were frozen to −79° C. by immersing the test-tubes containing the suspensions in a bath of ethanol and solid carbon dioxide. After freezing for 15 min., the cell suspensions were thawed by immersion in warm water (35° C.). The extent of hæmolysis was observed after sedimenting the undamaged cells in a centrifuge. The results of this experiment are shown in Fig. 1.

Bull semen was mixed with an equal volume of egg-yolk – citrate diluent[3] and cooled slowly during 1 hr. to + 4° C. Solutions of either dimethyl sulphoxide or glycerol in 0·16 *M* sodium chloride containing 0·1 per cent glucose, also at + 4° C., were then mixed with the suspensions of spermatozoa in the proportion 9 to 1. After 30 min. at + 4° C., to allow the permeation of the cells by the solutes, the suspensions contained in small test-tubes were frozen to − 30° C. and left at this temperature for 5 min. Part of the frozen suspension at − 30° C. was thawed and examined for motility and part was frozen further to − 79° C. After 15 min. at the lower temperature, the suspensions were thawed in warm water at + 35° C. and examined for motility. The results showed that dimethyl sulphoxide provided some protection against the damaging effects of freezing, but that, under the experimental conditions used, this was less than the protection afforded by glycerol. Motility persisted for several hours in 15 per cent dimethyl sulphoxide at room temperature, thereby suggesting that the toxicity of this solute, at least to spermatozoa, is low.

With both bovine and human red blood-cells, dimethyl sulphoxide penetrates the cells more rapidly than does glycerol and less of the solute is required for complete protection against damage by freezing. With bovine red blood-cells, the difference in rate of penetration was outstanding: 2 hr. equilibration with glycerol before freezing gave only poor protection whereas 30 sec. with dimethyl sulphoxide was sufficient for complete protection. Dimethyl sulphoxide does not, under the conditions used, appear to be as effective as glycerol in the protection of bull spermatozoa, but (in view of the sensitivity of this cell to freezing damage) the partial protection observed is of some interest and is shared by few other solutes[4].

A wide variety of living tissues can now be preserved in the frozen state through the protective action of glycerol; some, however, because of their large size or the impermeability of their membranes to glycerol are permeated by this substance so slowly that protection is slight. With this type of tissue, dimethyl sulphoxide, provided it proves to be otherwise harmless, may serve as an alternative protective agent.

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Ethylenediamine Tetraacetate and the Intestinal Absorption of Vitamin B_{12}

For the laboratory, as opposed to the clinical, analysis of the defective absorption of vitamin B_{12} in pernicious anæmia caused by the lack of Castle's intrinsic factor, several methods have been developed since radioactive preparations of the vitamin became available. In the first the absorption is studied by measuring the radioactivity of the fæces produced by gastrectomized rats given a test dose of labelled vitamin B_{12}, with or without an intrinsic preparation[1-3]. The defect of absorption in these animals closely resembles that found in pernicious anæmia in humans[4]. In a second method slices or homogenates of rat liver or strips of rat intestine are exposed to a preparation of hog intrinsic factor and simultaneously or afterwards to labelled vitamin B_{12}[5-7]. With this technically simpler *in vitro* method hog intrinsic factor was found to increase the uptake of vitamin B_{12} by the tissue preparation. This effect is dependent on the presence of calcium in the incubation fluid and can be abolished by the addition of ethylenediamine tetraacetate (as the disodium salt dehydrate) to the medium[8,9].

In this communication results on the effect of ethylenediamine tetraacetate on the intestinal absorption of radioactive vitamin B_{12} by gastrectomized rats are presented. We preferred the use of animals in which the entire stomach had been resected because in this way a possible influence of endogenous

Table 1. Fæcal Radioactivity expressed as a Percentage of the Test Dose in Gastrectomized Rats given 0·005 μgm. Vitamin B_{12}-^{58}Co + 0·5 ml. Neutralized Rat Gastric Juice, together with

1 ml. water	1 ml. 5 per cent EDTA*	1 ml. 10 per cent EDTA*
37	39	41
48	42	48
52	45	50
53	46	51
55	48	55
55	48	84
57	52	
57		
Mean : 52	46	55

* EDTA, ethylenediamine tetraacetate

intrinsic factor is excluded. The rats were given 0·005 µgm. vitamin B_{12}–^{58}Co and 0·5 ml. rat gastric juice with 1 ml. tap-water or 1 ml. 5 per cent or 1 ml. 10 per cent ethylenediamine tetraacetate solution by a thin rubber catheter introduced into the œsophagus.

The radioactivity of the fæces collected over the following four days was determined. The results summarized in Table 1 indicate that the large amounts of ethylenediamine tetraacetate, which were sufficient to cause diarrhœa in a number of animals, did not impair the intestinal absorption of vitamin B_{12}.

Apart from this lack of effect there are other points of disagreement between the results obtained with the *in vitro* method and the observations using gastrectomized rats. In the operated animal, rat gastric juice or rat stomach preparations are the only effective sources of intrinsic factor, while different hog intrinsic factor preparations are inactive[4]. The effect of hog intrinsic factor concentrates promoting the uptake of radioactive vitamin B_{12} by tissue preparations *in vitro* is not shared by rat gastric juice[10]. In the *in vitro* test, rat liver slices, which are exposed to a hog intrinsic factor concentrate and then washed prior to incubation with vitamin B_{12}, show an increased uptake, while in the gastrectomized rat intrinsic factor is active only when given simultaneously with labelled vitamin B_{12}[4]. The results of the *in vitro* experiments with rat liver slices are therefore difficult to evaluate when one attempts an analysis of the physiologically characteristic activity of the intrinsic factor which promotes the intestinal absorption of vitamin B_{12}.

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Role of Liver in Metabolism of Chlorpromazine

In previous studies[1] we demonstrated that the intact rat was capable of demethylating chlorpromazine-(N-methyl)-^{14}C when production of carbon dioxide was used as an index of demethylation. The liver seemed to be the likely tissue responsible for these findings, since Mueller and Miller[2] had found that homogenates of rat liver were capable of demethylation. La Du *et al.*[3] later developed a simpler system for demethylation using homogenates of rabbit, rat and guinea pig livers. However, using the system of La Du *et al.*, Salzman and Brodie[4] reported that no demethylation of chlorpromazine occurred with rabbit liver. Since we had observed the *in vivo* demethylation of chlorpromazine, we decided to study its *in vitro* demethylation by fortified homogenates of rabbit and rat liver prepared according to these procedures[2,3].

Non-fasted adult male rabbits (3·0–4·0 kgm.) and adult male Long Evans rats (225–250 gm.) were killed by a blow on the head, exsanguinated, and the livers were quickly removed. Homogenates of rat liver initially were made according to the procedure of Mueller and Miller, and fortified with their medium consisting of nicotinamide, adenosine triphosphate, di- and tri-phosphopyridine nuleotides, magnesium chloride, potassium chloride and phosphate buffer, *p*H 7·4, except that 0·12 µmole of glucose-6-phosphate was substituted for glucose-1,6-diphosphate. Rat livers were also homogenized according to the procedure of La Du *et al.*, and fortified with their medium consisting of nicotinamide, triphosphopyridine nucleotide, magnesium chloride and phosphate buffer, *p*H 7·4. The latter homogenates of rat liver were also fortified with the medium of Mueller and Miller. Homogenates of rabbit liver were prepared according to the procedure of La Du *et al.*, and fortified with their medium.

Incubations of labelled chlorpromazine with 33 per cent homogenates prepared according to the procedure of La Du *et al.*, and 10 per cent homogenates prepared according to the method of Mueller and Miller were conducted aerobically in closed vessels for 1 hr. at 37° C. in a Warburg apparatus. The supporting media contained 110–115 µgm. chlorpromazine and approximately 2·7 × 10^5 c.p.m. Liberated carbon dioxide was trapped as carbonate in 10 per cent sodium hydroxide solution in a centre well. At the end of incubation trichloracetic acid was added to the contents of the main chamber in order to liberate bound carbon dioxide. After another hour of incubation the carbonate in the centre well was precipitated as barium carbonate, and radioactivity was determined[1]. The influence of reagents or homogenates inactivated by heat on the liberation of the carbon-14 label was followed by incubating the complete medium with the solution used for homogenization or with homogenates heated at 100° C. for 5 min.

The results are reported in Table 1. Under the conditions of these experiments, it is evident that chlorpromazine-(N-methyl)-^{14}C was demethylated by homogenates of rabbit liver when adequately fortified. On the other hand, the labelled compound is demethylated by homogenates of rat liver prepared by either procedures for homogenization only when the medium of Mueller and Miller was used.

The ability of the liver to diminish the pharmacological activity of chlorpromazine by oxidation of the

Table 1. PRODUCTION OF CARBONATE-^{14}C FROM CHLORPROMAZINE-(N-METHYL)-^{14}C BY HOMOGENATES OF RABBIT AND RAT LIVER

Species	Ref. No. for preparation of homogenate	Ref. No. medium	Percentage of substrate-^{14}C recovered as $Ba^{14}CO_3$ Active homogenate	Boiled homogenate	Reagents
Rabbit	3	3	43·9–44·3	0·0005	0·0003
Rat	3	3	0·0004	0·0001	0·0003
Rat	3	2	40·1–40·2	—	—
Rat	2	2	33·8–33·9	0·0001	0·0001

sulphur atom of the phenothiazine nucleus was suggested by earlier observations. Salzman and Brodie[4] found that homogenates of rabbit liver yielded chlorpromazine sulphoxide, which is pharmacologically less active than the parent compound. More recently, Kamm *et al.*[5] observed that homogenates of the livers of guinea pigs, rabbits, dogs, mice and monkeys also produced chlorpromazine sulphoxide. The present findings re-emphasize the capacity of the liver to diminish the pharmacological activity of chlorpromazine since pharmacological testing in these laboratories showed that 2-chloro-[10-(methylaminopropyl)]-phenothiazine hydrochloride and 2-chloro-[10-(aminopropyl)]-phenothiazine hydrochloride were less active than chlorpromazine[6].

We wish to thank Dr. W. Holmes for his advice during the initial phases of these studies.

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Selective Permeability of Living Tissues to Carbonic Acid

RECENT investigations of the influence of carbon dioxide on the action of certain drugs[1] and on antibody fixation[2] have suggested that this substance may be able to diffuse freely through the cell membrane and thereafter modify from inside the reactivity of some specific receptors. It has been demonstrated by Arvanitaki[3] and more recently by Caldwell[4] that carbon dioxide can alter the intracellular *p*H of certain nerve and muscle fibres.

The following investigations provide evidence that carbonic acid diffuses rapidly through living tissues and membranes.

Experiments were carried out with carp (*Cyprinus carpio*) swim-bladder, rabbit bladder and guinea pig colon. The experimental apparatus is shown in Fig. 1. The inside of the organ was filled with Tyrode solution buffered with 1·2 m*M* $NaHCO_3$ and adjusted to *p*H about 7·2. The liquid outside the membrane was a Tyrode solution buffered either with $NaHCO_3$ (1·2 m*M*) or with sodium maleate (12 m*M*). In the first case, the *p*H was adjusted to 4·8 by saturation with carbon dioxide, while in the second case the *p*H was lowered to the same value by addition of the proper quantity of maleic acid. The *p*H of the internal solution was measured potentiometrically at different times. Experiments with the fish swim-bladder were performed at room temperature (18 ± 2° C.) while those with mammalian tissues were carried out at 37° C.

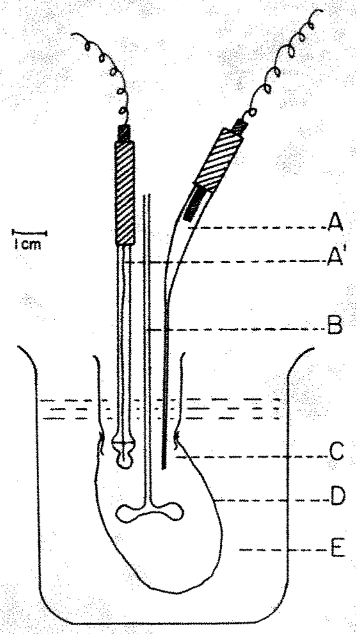

Fig. 1. Experimental apparatus. *A* and *A'*, electrodes; *B*, mixer; *C*, internal solution; *D*, membrane; *E*, external solution

When the *p*H of the external solution was lowered by saturation with carbon dioxide, a gradual decrease of the *p*H of the internal solution was regularly observed. On the contrary, when the external solution was acidified with maleic acid, no significant changes of the *p*H of the internal solution were observed. A typical experiment is represented in Fig. 2. Similar negative results were obtained by acidification of the external solution with acetic, benzoic, succinic or hydrochloric acids: none of these acids was able to acidify the solution on the other side of the membrane.

In certain experimental conditions the *p*H of the internal solution can be brought down to a level which is lower than that of the external one. That happens when the external Tyrode solution is buffered with 60 m*M* $NaHCO_3$ and saturated with carbon dioxide. The result of such an experiment is presented in Fig. 3.

Experiments performed by acidifying the internal fluid have proved that the behaviour of the tissue

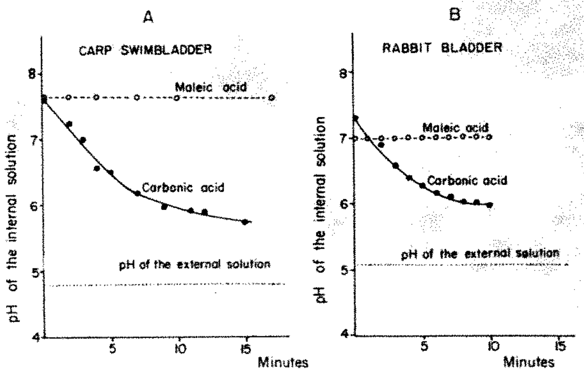

Fig. 2. Modifications of the *p*H of the internal solution after acidification of the external solution with carbonic acid or with maleic acid

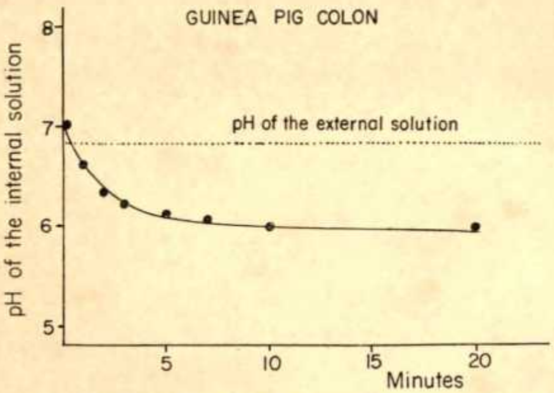

Fig. 3. Modification of the pH of the internal solution after saturation with carbon dioxide of the external solution, buffered with 60 μmol./l. of $NaHCO_3$

is very similar: acidification of the external solution was observed with carbonic acid but not with maleic acid.

These results suggest that carbonic acid can pass through the living membrane and cause the acidification of the internal medium. It can be postulated that what occurs with such complex tissues as the bladder or colon may also occur with single cells. But this remains to be proved. The selective permeability of carbonic acid has not been observed with artificial membranes such as 'Cellophane' tubing, and in this case the movements of the acids obey the general laws of simple diffusion.

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Distribution of 5-Hydroxytryptamine in Scorpion Venoms

IN previous communications[1,2] the occurrence of high concentrations of 5-hydroxytryptamine in the venom of *Leiurus quinquestriatus* was reported. Since then, the venom of *Buthotus minax* L. Koch (another common local species) has been found to contain much smaller amounts of 5-hydroxytryptamine, and this observation has been correlated with the histological appearance and histochemical reactions of the venom glands.

The method of obtaining venom and its subsequent treatment has been described previously, as have the histological methods used[1,2]. The venoms of both *B. minax* and *L. quinquestriatus* were obtained over the same period of the year, and estimations of the 5-hydroxytryptamine content were made on the pooled venom of each. Sections of venom glands were prepared at the same time, and treated simultaneously. The assay of 5-hydroxytryptamine was carried out on the fundus of the rat's stomach by Vane's method[3]. This preparation is particularly sensitive to 5-hydroxytryptamine and is also relatively specific for this substance in the presence of hyoscine (10^{-7} gm./ml.). Specificity was also tested by antagonizing venom-induced contractions with 2-bromo-lysergic acid diethylamide (5×10^{-6} gm./ml.) (we are indebted to Sandoz, Ltd., Basle, for a gift of 2-bromo-lysergic acid diethylamide).

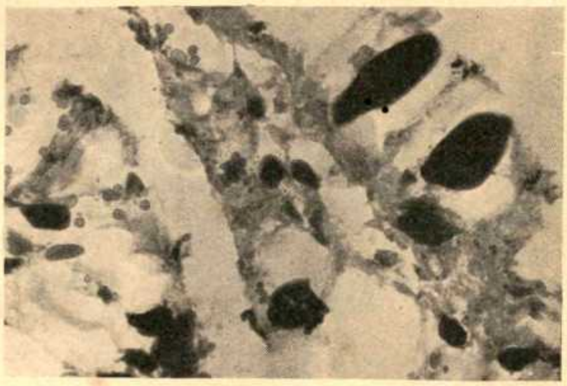

Fig. 1. *L. quinquestriatus* venom gland, 10μ, argentaffin reaction with Fontana's ammoniacal silver method. (× 400)

Assays of the venom of *B. minax* on the fundus of rat's stomach indicated a concentration of 0·03–0·04 μgm. 5-hydroxytryptamine/mgm. dry weight of venom. Paper electrophoretic separations when treated with acid ninhydrin[4] showed no fluorescence in ultra-violet light. Estimates of 5-hydroxytryptamine in the venom of *L. quinquestriatus* on the rat fundus preparation confirmed the previously reported concentration of 2–4 μgm. 5-hydroxytryptamine/mgm. of dry venom.

The general organization of the venom gland of *B. minax* is similar to that of *L. quinquestriatus*; but the rather prominent coarse granules that appear in the latter gland after formalin fixation are much less abundant in the case of *B. minax*. A high proportion of these coarse granules in the glands of *L. quinquestriatus* are argentaffin (Fig. 1), whereas no argentaffin structures were seen in the case of *B. minax* (Fig. 2). Similarly, in sections of *L. quinquestriatus* granules which give a positive diazo reaction with fast red salt *B* are seen, but in sections of *B. minax* the diazo reaction is negative. Distinct yellow-green fluorescence in ultra-violet light was observed in a proportion of the coarse granules and some fine-granular cells in *L. quinquestriatus*. No fluorescence was seen in sections of the glands of

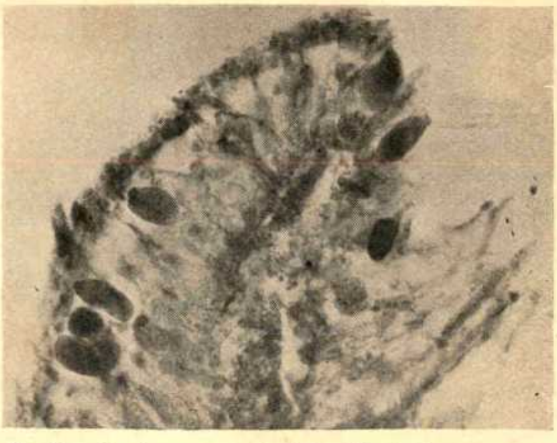

Fig. 2. *B. minax* venom gland, 10μ, Fontana's ammoniacal silver method. (× 450)

B. minax. The indole reaction was marked in many cells in sections from *L. quinquestriatus* glands ; but sections from *minax* glands showed only a few faintly positive structures. This reaction does not appear to be so specifically connected with the coarse granules as are the other histochemical methods used, but seems to spread throughout whole cells, which exhibit a very fine granular structure. These same cells give a positive Sakaguchi reaction for arginine.

Sections of venom glands of *Parabuthus hunteri* (a less common species here) have also been examined and found to show the same structure and histochemical reactions as do sections from glands of *L. quinquestriatus* but in much less-marked fashion. 5-Hydroxytryptamine is present in this venom in sufficient quantity to produce fluorescence after treatment with acid ninhydrin ; but insufficient venom has been available so far to give a reliable estimate of the content of 5-hydroxytryptamine.

It seems remarkable that species of the same family (Buthidae) should show such a marked difference in the 5-hydroxytryptamine content of their respective venoms, that of *B. minax* being about one hundredth of that found in *L. quinquestriatus*. So far as can be observed, *minax* venom is as effective in its normal function of paralysing active prey as is the venom of *L. quinquestriatus*, and this leads to speculation as to whether the 5-hydroxytryptamine in venom serves any biologically useful purpose. It can undoubtedly contribute largely to the pain caused by a scorpion sting (Adam and Smith, unpublished observations) and this has been suggested as being of survival value (cf. Collier[5]). Nevertheless, *B. minax* seems capable of surviving well enough though its venom has the reputation of being less toxic to man than is that of *L. quinquestriatus*, and this may well be attributed partly to the lower content of 5-hydroxytryptamine and partly to the fact that *minax* is a smaller scorpion and has a smaller quantity of venom at its disposal. However, the various current hypotheses of the normal function of 5-hydroxytryptamine, which include a possible neurohumoral role in some invertebrates and an action as a central transmitter in mammals (cf. Page[6]), tend to persuade one that the presence of 5-hydroxytryptamine in venoms is not entirely fortuitous.

In a previous paper[2], it was reported that cells of venom glands of *L. quinquestriatus* did not always show clearly positive enterochromaffin reactions[7]. In the present work all the typical enterochromaffin reactions were found to be strongly positive. A possible explanation for these differences may be that the production of 5-hydroxytryptamine by the venom glands varies at different times of the year. However, such a variation in the 5-hydroxytryptamine content of the venom could not be found since estimations of it were carried out on venom which was collected and pooled over periods of several months. The sections of *B. minax* and *L. quinquestriatus* glands were made at the same time of the year and treated simultaneously, and therefore, from this point of view, comparison is valid. Only faintly positive results to the enterochromaffin reactions were obtained with *B. minax* sections. This correlates well with the contrast in 5-hydroxytryptamine contents of the respective venoms and adds further weight to the concept that cells showing enterochromaffin reactions are producers or storers of 5-hydroxytryptamine.

The indole reaction is much less specific ; but in this case the strongly positive result obtained with *L. quinquestriatus* sections probably indicates that the reaction occurred with 5-hydroxytryptamine or its precursors, since a very weak reaction was seen in sections of *B. minax*, and since the other constituents of the two venoms seem to be similar (Adam and Weiss, unpublished observations).

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An Effect of Insulin on Peptide Synthesis independent of Glucose or Amino-Acid Transport

Insulin enhances incorporation of amino-acids labelled with carbon-14 into protein of isolated rat diaphragms independent of its action in facilitating entry of glucose[1–3]. Kipnis and Noall[4] report that in similar circumstances insulin increases the accumulation of ^{14}C-α-amino*iso*butyric acid, a non-utilizable amino-acid. If the rate of penetration of the utilizable labelled amino-acids is also increased by insulin, the result would be a rise in the radioactivity of the intracellular amino-acid pool. Then an apparent increase in the rate of incorporation could occur without an actual change in the rate of peptide synthesis. This possibility has now been tested. Increased transport does not account for the insulin-mediated increase in the incorporation of utilizable amino-acids.

The method adopted was to divorce penetration and incorporation by effecting amino-acid accumulation before adding insulin. The amino-acid labelled with carbon-14, instead of being added *in vitro*, was injected intraperitoneally into the diaphragm donor ; 10 min. later the rat was killed and the diaphragm removed and pre-soaked (at 0–5° C.) for 20 min. in 10 ml. of Krebs–Henseleit bicarbonate medium without glucose. Presoaking in a large volume of fluid allows equilibration of the extracellular glucose and amino-acids with that in the medium. One hemi-diaphragm was then gently blotted and transferred to a beaker containing 1 ml. of medium without glucose. The second hemi-diaphragm was placed in 10 per cent trichloracetic acid ; it served as a zero-time control. Incubation was for 2 hr. at 37° C. in a Dubnoff shaker. At the conclusion of the experiment the muscle protein was isolated and its radioactivity determined[2] ; this is a measure of incorporation of amino-acid into peptide linkages (that is, protein synthesis).

Four experiments were carried out ; representative results are given in Table 1. Insulin added *in vitro* (0·2 unit/ml.) leads to a large increase in the incorporation of DL-phenylalanine-3-^{14}C and DL-histidine-2-^{14}C into muscle protein. This increase occurred despite accumulation of amino-acid having been effected before insulin was added and despite the absence of added glucose in the medium. The stimulation by insulin was larger than that obtainable when the amino-acid was added to the medium[3].

Table 1. Effect of Insulin on Incorporation of Amino-acid Labelled with Carbon-14 into a Protein Fraction of Diaphragms from Normal Fed Rats

Labelled amino-acid	No insulin			Insulin		
	C.p.m./mgm. of protein			C.p.m./mgm. of protein		
	0	2 hr.	Difference	0	2 hr.	Difference
Phenyl-alanine	70	159	89	72	218	146
	65	153	88	78	230	152
	85	148	63	70	220	150
	57	160	103	55	197	142
	54	122	68	57	198	141
				77	242	165
				38	176	138
	Mean		82			148
Histidine	11	45	34	9	72	63
	12	46	34	9	75	66
				14	91	77
	Mean		34			69

The DL-phenylalanine-3-^{14}C (1·3 mc./m*M*) and the DL-histidine-2-^{14}C (1·0 mc./m*M*) were injected in 0·25 ml. of normal saline (1×10^7 c.p.m.). The control (no insulin) and experimental (insulin) groups were run simultaneously. The insulin (0·2 unit/ml.) was added *in vitro*. The results are expressed as c.p.m., corrected for self-absorption, per mgm. of protein isolated (usually 15–20 mgm.). Results in the zero column represent incorporation prior to the start of incubation as determined in one hemi-diaphragm; the 2-hr. column, results after the incubation period. The difference is the net increase in amino-acid incorporation during the experiment. *N.B.* In each experiment insulin mediates a large increase in amino-acid incorporation.

Control experiments demonstrated that only a small fraction of the labelled amino-acid incorporated either in the presence or absence of added insulin could have been derived from the extracellular fluid. The radioactivity in the Krebs–Henseleit medium in which the diaphragms were presoaked was determined. In one experiment with phenylalanine labelled with carbon-14 this was found to be 2,996 c.p.m./ml. of medium (range 2,610–3,310); in an experiment with labelled histidine it was 2,910 c.p.m./ml. of medium (range 2,638–3,239). The radioactivity in the Krebs–Henseleit medium is presumed to be in equilibrium with the extracellular fluid of the diaphragm, and this represents the maximum amount of radioactivity which can be carried over into the incubation medium. The wet weight of each hemi-diaphragm was approximately 100 mgm. (weight of the rats 110–130 gm.), and if we assume an extracellular space of 35 per cent of wet weight[5] the extracellular volume is 0·035 ml. We can now calculate that the radioactivity present in the extracellular fluid of the diaphragm is 105 c.p.m. (that is, 3,000 c.p.m./ml. × 0·035 ml.). The total observed increase in protein radioactivity in the phenylalanine experiment was 1,562 ± 114 (standard error) without insulin and 2,494 ± 127 with insulin; in the histidine experiment the values were 679 ± 47 and 1,336 ± 74 respectively. It is apparent that contamination of the extracellular fluid with administered labelled amino-acid could not account for the observed results.

We conclude from these preliminary results that insulin can influence protein synthesis at a locus distal to amino-acid penetration and independent of glucose entry.

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Failure of Ribonucleoprotein to transfer Antibody Formation

Some data[1] indicate that templates for antibody synthesis consist of a ribonucleoprotein. Šterzl and Hrubešova[2], and Hrubešova *et al.*[3] have found that infant rabbits form antibodies when injected with nucleoproteins isolated from the spleen of immunized donors. However, they were not able to prove that those antibodies originated *de novo*.

Chickens are excellent producers of precipitins, and spleen forms antibodies at a high rate showing an increase in pentose nucleic acid and cells of the plasmocytic series[4]. On the other hand, Coombs's anti-human globulin test has proved to be extremely sensitive in detection of Rh antibodies. The present work combines these data in an investigation of the capability of ribonucleoprotein from an antibody-producing tissue to provoke antibody formation when transferred into infant chicks. This preliminary communication represents only one part of the results obtained.

Fifty Rhode Island Red pullets and infant chicks were used in the experiments. Adult chicks were immunized with human γ-globulin[5], the spleens removed three days after the last injection of antigen and used as a source of ribonucleoprotein. The titres of anti-human globulin antibody in the sera of killed birds were 1/1,000–3,000, as determined by Coombs's technique, using O CDe/CDe red cells strongly sensitized in an anti-D serum. (The same sensitized red cells were used in Coombs's test throughout the experiments.) The preparation of ribonucleoprotein was as follows. Spleens were removed, decapsulated and quickly frozen. Cytoplasmic homogenate was prepared in 0·14 *M* saline (1 gm. tissue to 2 ml. saline), left at 0° C. for a period of 3 hr. and then spun in a refrigerated centrifuge at 3,000 r.p.m. for 20 min. to remove large particles. The supernatant was dialysed against redistilled water overnight. The proteins were precipitated by cold ethanol (−10° C.), centrifuged and redissolved in 0·14 *M* saline. The method of Lowry *et al.*[6] was used for protein determination, and the concentrations of ribonucleic acid and deoxyribonucleic acid were determined according to Mejbaum's[7] and Ceriotti's[8] methods respectively. Ultra-violet light absorptions were measured in a Beckman *DU* spectrophotometer. 1 ml. of ribonucleoprotein preparation contained 5·3 mgm. protein, 1·03 mgm. ribonucleic acid and 0·027 mgm. deoxyribonucleic acid.

No evidence for the detectable quantity of anti-human globulin antibody and human γ-globulin in the ribonucleoprotein preparation was obtained. The following methods were used: (*a*) the capillary precipitin method with varied final salt concentrations[9]; (*b*) a modification of Ouchterlony's double-diffusion agar precipitin technique[10]; (*c*) the inhibition effect of ribonucleoprotein on an anti-human globulin serum with a low titre of specific antibody; (*d*) the Coombs's test performed with different dilutions of ribonucleoprotein complex; (*e*) examination for anti-human globulin antibody in the sera of six-month-old chicks which had received subcutaneously several injections of ribonucleoprotein.

One group of birds received intraperitoneally 2 ml. of ribonucleoprotein on the fifth day, and the second group on the twelfth day of post-embryonic life. The animals were bled on the first, third, sixth and tenth day later, and Coombs's tube technique was performed for detection of anti-human globulin antibody in chick sera. Each serum was used in different dilutions against a series of differently sensitized red cells. The following controls were set up: (*a*) Coombs's test with infant chick sera obtained prior to injection of ribonucleoprotein; (*b*) Coombs's test and capillary precipitin reaction performed with sera of infant chicks which had been treated with human γ-globulin (10-day-old chicks received four injections of 16 mgm. globulin during a period of 12 days); (*c*) Coombs's test with sera from adult chicks which had been intravenously injected with ribonucleoprotein (the heteroagglutinins for human red cells were removed by absorption).

All results obtained with the sera from treated infant and adult chicks were negative, showing no presence of circulating anti-human globulin antibody. The temporary unresponsiveness of chick infants to human γ-globulin (control *b*) is probably due to the immunological and protein-synthesizing immaturity of those cells which would later be responsible for production of antibodies. It seems, however, that the failure of ribonucleoprotein to induce the formation of antibodies in infant (test groups) and adult (control *c*) recipients also concerns the catabolic rate of ribonucleic acid when injected into animals of the same species. This facet of the problem was partly investigated by the method of Rabinovitch and Dohi[11] for the detection of serum ribonuclease, and the presence of this enzyme in the sera of treated infant and adult birds was established. This represents, of course, only indirect evidence for the interference of ribonuclease. But, since the integrity of ribonucleic acid is essential for protein synthesis[12], this possibility should be taken into account. Mention should also be made of the fact that the present work deals with cytoplasmic ribonucleic acid, and that different results may probably be obtained with nuclear ribonucleic acid owing to its higher specific activity[13]. Finally, whatever the correct interpretation might be, more observations are obviously needed about the fate of the isolated ribonucleoprotein and ribonucleic acid when injected into animals, and about the ability of molecules of ribonucleoprotein and ribonucleic acids to be incorporated by protein-synthesizing mechanisms of the recipient. It might be added that, in this respect, one is faced with essentially different situations when working with intact antibody-producing cells.

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Neurosecretion and Intestinal Proteinase Activity in an Insect, *Calliphora erythrocephala* Meig.

SOME years ago it was suggested that the medial neurosecretory cells of the brain of *Calliphora erythrocephala* in some way influence protein metabolism, and especially the synthesis of protein. This hypothesis was based on the fact that in females deprived of these cells, the ovaries, accessory glands, corpora allata and œnocytes, organs which normally increase considerably in size during the early period of adult life, developed to a limited extent only although the flies were given an adequate diet of meat, sugar and water[1,2]. Furthermore, in flies fed on sugar and water only, but no meat, the organs mentioned were very nearly the same size as in females deprived of their medial neurosecretory cells. Therefore it seemed likely that in the absence of the hormone from the medial neurosecretory cells for some unknown reason the fly was unable to utilize the ingested meat. Observations proved that the flies did in fact eat some of the meat offered to them.

Transport of neurosecretory material in the two nervi œsophagei, which pass from the corpus cardiacum + ganglion hypocerebrale to the intestine, was described earlier[3,4]. This neurosecretory material is probably produced by the medial neurosecretory cells. Cutting the nerves caused a definite retardation of the growth of the ovaries[1]. These observations suggest an influence of the medial neurosecretory cells on digestion. This possibility was tested in experiments reported here.

For the determination of the proteinase activity of the gut we used the colorimetric method of Day and Powning[5], originally described by Charney and Tomarelli[6], but the homogenates were kept for four hours in the incubator instead of one. According to this method the intestines were ground in small tubes with clean sand which had been moistened with a glycerin–phosphate buffer mixture[7]. After homogenization, which was performed at room temperature, the volume of fluid in each tube was made up to 1 ml. with buffer solution. The tubes were kept overnight in the refrigerator. The flies used were females deprived of their medial neurosecretory cells when 5–8 hr. old (25° C.), operated controls[1], and normal, that is, unoperated controls. After the operation the flies were kept for 5 days at 25° C. and fed on meat, sugar and water. Some determinations were made on females fed only on sugar and water for 5 days, called sugar-flies.

Wigglesworth[8] found the proteinase activity of the midgut of *Calliphora* to be very weak as compared with that of *Glossina*. Apart from the sugar-flies our flies were given fresh meat for 2 hr. before the intestines were removed, and they were not starved before they had this last meal. Only the abdominal portion of the midgut was used for the determinations, and it was recorded whether or not the flies had eaten some of the fresh meat. The midguts were dissected 2½–6½ hr. after the beginning of the last meal. Probably we would have obtained higher values if the determinations had been undertaken some hours later[9]. As the determinations were made on homogenates of the midguts, the enzymatic activity of both the intestinal content and the intestinal cells was measured. The values are calculated per midgut, and not by weight of midgut, because in starved, normal flies with an empty gut the values were

Table 1. PROTEINASE ACTIVITY PER MIDGUT OF FEMALES DEPRIVED OF THEIR MEDIAL NEUROSECRETORY CELLS, OPERATED CONTROLS, NORMAL (UNOPERATED) CONTROLS AND SUGAR-FLIES. FIVE DAYS OLD AT 25° C. A MATURE EGG IS ABOUT 1·45 MM. LONG

Deprived of medial neurosecretory cells		Operated controls		Normal controls		Sugar-flies	
Proteinase (optical density × 10^2)	Length of biggest egg-chamber (mm.)	Proteinase (optical density × 10^2)	State of ovaries	Proteinase (optical density × 10^2)	State of ovaries	Proteinase (optical density × 10^2)	Length of biggest egg-chamber (mm.)
0·4	0·13	3·3	almost mature	1·5	mature	0	0·12
0·4	0·15	5·0	laid eggs	2·2	mature	0·1	0·12
0·5	0·13	6·0	almost mature	5·0	¾ mature	0·1	0·13
0·7	0·12	7·4	¾ mature	5·1	almost mature	0·1	0·13
0·9	0·15	8·5	⅔ mature	5·5	½ mature	0·1	0·15
1·4	0·13	9·5	⅓ mature	5·7	almost mature	0·4	0·15
1·4	0·13			6·8	4/5 mature	0·6	0·15
1·6	0·12			8·0	laid eggs	0·6	0·13
1·7	0·15			9·6	¾ mature	1·1	0·13
1·9	0·15			14·8	⅓ mature	1·9	0·08
1·9	0·15			15·0	½ mature	1·9	0·10
2·7	0·15						

found to be of the same order as in flies lacking medial neurosecretory cells.

Formerly it was found that in females deprived of their medial neurosecretory cells the length of the biggest egg-chamber never exceeded 0·17 mm., and therefore the size of the longest egg-chamber was used as a control on the removal of the cells. The stage of development of the ovaries of the operated and normal controls and of the sugar-flies was also noted.

The proteinase activity in the four categories of flies is given in Table 1. Apart from two normal controls with fully mature ovaries, the midguts of the operated controls and those of the normal controls had a much higher proteinase activity than the midguts of the flies deprived of medial neurosecretory cells. As the midguts of most of the flies contained meat, the figures do not merely give the values of the proteinase activity of the intestine itself but also the activity of the intracellular proteinases of the meat, but whatever its size it should be the same in all sets of animals.

In *Aedes aegypti* Shambough[10] found a pronounced correlation between the amount of ingested blood and the proteinase activity. So far it has not been determined whether blow-flies deprived of medial neurosecretory cells eat less meat than the controls. But even if there is a similar correlation in the normal *Calliphora* as in *Aedes*, this does not seem to apply to flies deprived of medial neurosecretory cells, because these flies, in spite of having ingested meat, do not show a higher proteinase activity than the sugar-flies. The speed at which the food travels through the intestine[11] might also be a significant factor.

As proteinases are themselves proteins, the production of proteinase by the intestinal cells can be regarded as the protein synthesis of these cells, and so the result of this investigation seems to support the view that the hormone from the medial neurosecretory cells has an influence on the protein metabolism, and especially on the synthesis of protein. If *Calliphora* without medial neurosecretory cells is able neither to break down nor build up protein, it is easy to understand why the removal of the cells produced a result in a 100 per cent of the flies. It also explains the small variation in the size of the growing organs[1].

As pointed out earlier[1] the flies deprived of medial neurosecretory cells are able to utilize the specific protein of the larval fat-body, part of which is carried over into the adult stage where it is used for the small initial growth of the organs which do grow in the adult (see above). This fact seems to agree with our interpretation of the function of the neurohormone. Welsh and Travis[12] have substantiated the view that another neurohormone, namely, the neurohumor acetylcholine in Planaria, is involved in growth and tissue maintenance.

As yet we do not know whether the effect of the neurohormone on the production of intestinal proteinase is a direct or an indirect one. The investigation is being continued, and a more detailed account of the experiments will be published elsewhere.

It is a pleasure to thank Prof. H. Holter for valuable discussions. We also wish to thank the Carlsberg Foundation, which has supported this work with a grant.

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Utilization of Inorganic Sulphate by Baker's Yeast

IT has been established by a number of authors that sulphate is the usual source of sulphur for many micro-organisms, and also for yeasts[1]. However, much remains to be elucidated about the details of sulphate uptake by the cell and its metabolism.

We have examined the conditions of transport of sulphate into *Saccharomyces cerevisiae* and the effect of several other sulphur-containing compounds thereon. Throughout the work, washed baker's yeast was used, which was shaken for 5 hr. in an inorganic

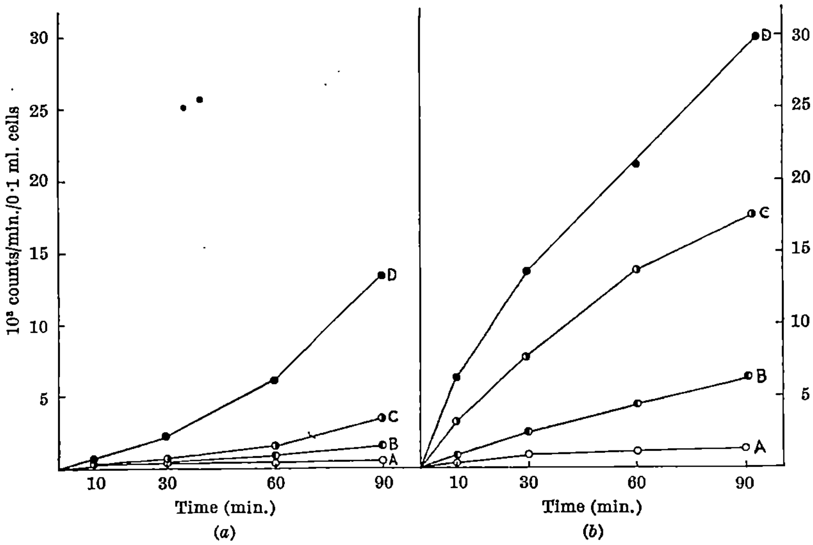

Fig. 1. Incorporation of radioactive sulphate in a nitrogen-deficient (left) and a sulphur-deficient (right) yeast. Incubation in air at 22°. *A*, Medium without glucose and ammonium chloride; *B*, medium without glucose; *C*, medium without ammonium chloride; *D*, complete medium

salt medium enriched with yeast extract; from the complete medium either ammonium chloride or potassium sulphate was omitted and thus nitrogen-deficient and sulphur-deficient yeast were obtained, respectively. Incubation of the washed yeast was then carried out aerobically at 22° in the same inorganic medium but without yeast extract and with ammonium chloride or glucose or both omitted as required. An osmotically insignificant amount of $^{35}SO_4^{2-}$ was added to trace the incorporation of sulphur into various yeast components. Samples of the suspension were centrifuged at 0°, washed with ice-cold water and aliquots used for determining the total radioactivity of cells and the radioactivity of the supernatant after hydrolysis of the cells in 5 *N* hydrochloric acid, removal of inorganic sulphate by precipitation with barium chloride and chromatography in butanol–acetic acid. No loss of radioactivity occurred during the washing procedure at 0°.

It follows from Fig. 1 that both glucose and ammonia are required for the maximum uptake of sulphate from the medium; thus both simple diffusion and active transport of sulphate into the cells appears unlikely. In nitrogen-deficient yeast a source of nitrogen in the medium is of decisive importance for the incorporation of sulphur-35 to occur, which is in agreement with the finding[2] that such yeast has its metabolic pool of nitrogen exhausted. On the other hand, in sulphur-deficient cells the nitrogen content is probably increased (*inter alia* due to depletion of glutathion sulphur, cf. ref. 3 for *E. coli*) and thus on adding sulphate to the medium sulphur-containing compounds may be formed without any exogenous source of nitrogen. Moreover, the lack of sulphur in the latter yeast brings about a more rapid uptake of radioactive sulphate. The steeper slope of curves *C* and *D* in both graphs is caused also by an actual increase in yeast dry solid (mainly polysaccharides under our experimental conditions). Essentially the same results were obtained by estimation of the decrease of sulphate content in the medium by chemical methods.

It was shown afterwards that at 0° no uptake of sulphate by the cells occurs. On varying the concentration of sulphate in the medium between 0·4 m*M* and 2·0 m*M* no change in the rate of sulphate uptake can be observed for the first hour of aerobic incubation of nitrogen-deficient yeast. These results also make simple diffusion of sulphate into the cell very unlikely.

Table 1. EFFECT OF SULPHUR-CONTAINING COMPOUNDS* ON INCORPORATION OF $^{35}SO_4^{2-}$

Compound added	Inhibition (per cent)	
	N-deficient yeast	S-deficient yeast
Na_2SO_3	58	38
$Na_2S_2O_3$	44	30
Thioglycollic acid	15	8
Cysteine	37	18
Methionine	16	8

* In each case 750 μgm. sulphur/10 ml. of medium was added

The effect of sulphur-containing compounds on incorporation of radioactive sulphate during aerobic incubation in a complete medium at 22° is shown in Table 1.

The Lineweaver–Burk plot of a kinetic measurement of sulphite and thiosulphate inhibition with sulphur-deficient yeast indicates that thiosulphate acts as a competitive inhibitor of sulphate uptake; sulphite, however, behaves somewhat anomalously at concentrations greater than 1 m*M* (cf. ref. 4). The generally higher inhibition in nitrogen-deficient yeast points to a more pronounced metabolic character of sulphur incorporation in such yeast; the details, however, are being studied at present.

The distribution of activity in amino-acids is rather complex, the general observation being only that methionine becomes active later in the course of incubation than cysteine. It appears from the results that most of the sulphate is not taken up as such by the yeast but rather in connexion with some nitrogenous carrier (for example, 3′-phospho-adenosine-5′-phosphosulphate[5]) and then metabolized further.

A detailed study of the effect of anaerobiosis and of inhibitors at various concentrations, particularly on individual amino-acids, is being concluded and will be published elsewhere.

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An Effect of Yeast Extract on the Growth of *Chlorella*

Chlorella vulgaris (Pearsall's strain) grows well on glucose in darkness[1]. Recently, in this laboratory, we tried to grow this alga on glucose in darkness in an atmosphere free from carbon dioxide. The attempt was unsuccessful; presumably carbon dioxide fixation is essential in at least one of the reactions necessary for growth. Since it has been reported that the requirement for carbon dioxide by *Neisseria gonorrhoeae* can be replaced by a supplement of yeast extract[2], the effect of adding yeast extract to the *Chlorella* cultures was investigated.

Pure cultures of *Chlorella* were grown in 50-ml. Erlenmeyer flasks in a mineral salts medium[3] containing 0·5 per cent glucose and 'Difco Bacto' yeast extract in the required concentration. The flasks contained a centre well, in which sodium hydroxide and filter paper were placed to remove carbon dioxide, and were closed by vaccine stoppers. The cultures were shaken at 25° C. in darkness. Growth was estimated by counting the cells four days after inoculation; it was expressed as a percentage of the growth in the cultures with glucose, no yeast extract and an atmosphere of air.

It was found that the addition of yeast extract did, in fact, allow some growth in a carbon dioxide-free atmosphere (Fig. 1); but the more striking effect of yeast extract was the inhibition of growth in an atmosphere of air. The growth of *Chlorella* on glucose in darkness, in air, was reduced by one-half by yeast extract in a final concentration of only 0·01 per cent. The inhibition was just as pronounced when the yeast extract was sterilized by Seitz filter and added to the autoclaved medium. The constituent of the yeast extract which inhibits growth is unknown. Organic acids inhibit the growth of *Chlorella* by combining with iron[4]. The possibility that a constituent of yeast extract acted in this way was tested by adding additional iron to the medium, but it had no effect on the inhibition.

It is of interest that a related, but colourless, alga, *Prototheca zopfii*, requires thiamine for growth[5] and, in fact, grows well in the *Chlorella* mineral medium with the addition of 1 per cent glucose and 1 per cent yeast extract. Removal of carbon dioxide from the atmosphere has little effect on the growth of *Prototheca* in this medium or when $10^{-5} M$ thiamine is substituted for the yeast extract (Table 1). This suggests either that *Prototheca* has a much lower carbon dioxide requirement for growth than *Chlorella*, or that thiamine can replace this requirement. However, the addition of $10^{-5} M$ thiamine to *Chlorella* cultures did not allow growth in a carbon dioxide-free atmosphere.

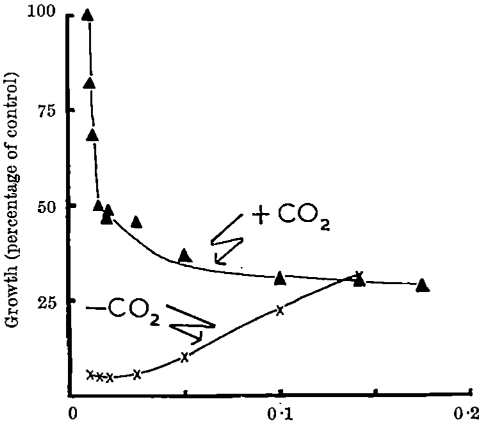

Fig. 1. The effect of yeast extract on the growth of *Chlorella vulgaris*. All cultures contained 0·5 per cent glucose and were shaken in darkness. The carbon dioxide-free cultures contained sodium hydroxide in centre wells of the flasks. Growth is expressed as a percentage of that in the flask with glucose, no yeast extract and an atmosphere of air

Table 1. GROWTH OF *Chlorella* AND *Prototheca* WITH AND WITHOUT CARBON DIOXIDE IN THE ATMOSPHERE

	Cells/c.mm.			
	Chlorella vulgaris (Pearsall's strain)		*Prototheca zopfii* (Beijerinck's strain)	
	+ CO_2	− CO_2	+ CO_2	− CO_2
No addition	12,320 (100%)	2,960 (24%)	—	—
1 per cent yeast extract	4,176 (34%)	3,430 (28%)	12,400 (100%)	12,501 (101%)
10^{-5} Thiamine	20,760 (168%)	3,135 (25%)	10,310 (83%)	11,500 (93%)
Inoculum	863 (7%)		79 (0·6%)	

Each flask contained 10 ml. of *Chlorella* mineral medium with 1 per cent glucose added and the other additions indicated. After inoculation the flasks were shaken in the dark at 25° C. in a Warburg tank. The carbon dioxide-free cultures contained sodium hydroxide in centre wells.

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Isolation of *l*-Quinic Acid in Citrus Fruit

THE organic acids in citrus juices are chiefly citric and malic, although tartaric and oxalic acids also have been reported in grapefruit[1]. In our laboratory, succinic acid was found in frozen mature oranges. Wolf[2] isolated citric, malic and an unidentified acid from citrus fruit. Sinclair and Eny[3] reported that in the peel malic acid predominates while citric and oxalic acids occur in smaller amounts.

In a study of organic acids in citrus fruit using the gradient elution technique on a 'Dowex-1' column, an unknown acid with an R_{malic} of 0·56 was detected in both the peel and juice. This acid alone or with authentic quinic acid was eluted from the column in the same fractions as quinic acid, and gave a positive test with the Cartwright and Roberts[4] reagent. The presence of *l*-quinic acid has been reported in apples[5] and peaches[6].

The quinic acid was first isolated from 1,600 gm. of immature Valencia orange peel using an ion-exchange resin, 'Dowex-1 × 8', of 200–400 mesh packed in a 2·3 cm. × 25 cm. column. The macerated peel was extracted three times with 60 per cent ethanol which was then evaporated under reduced pressure. The remaining aqueous solution was treated with charcoal, filtered, and first passed through a column of 'Dowex-50' ion-exchange resin and then through a column of 'Dowex-1' in the acetate form. This column was washed with distilled water, and the acid was eluted according to the gradient elution method of Hulme and Wooltorton[7] with a slight modification. The change consisted of using a 500-ml. mixing flask filled with water and gradually adding 2 N acetic acid during the elution. Fractions of 20 ml. were collected at 40 ml./hr. with a mechanical fraction collector. Each fraction was chromatographed on Whatman No. 1 paper with butanol–acetic acid–water (4 : 1 : 5). Quinic acid was detected with the Cartwright–Roberts[4] spray reagent in fractions 12 to 22, which were combined and evaporated to near dryness under reduced pressure. The residue was dissolved in 100 ml. of ethanol and precipitated by adding 4 vol. of ethyl ether. The crude quinic acid (2·5 gm.) recrystallized twice from ethanol produced 1·5 gm. of pure material. Apart from its chromatographic properties similar to quinic acid, the isolated compound had a melting point of 162° C. (ref. 8, 162° C.), which was not depressed when mixed with authentic quinic acid : $[\alpha]_D^{23} = -43°$ (ref. 8, $[\alpha]_D^{20} = -44°$) ; neutralizing equivalent, 195. Infra-red absorption was also similar to that of an authentic sample of quinic acid.

Table 1. QUINIC ACID IN MATURE CITRUS FRUIT

Variety and type of citrus fruit	Peel (mgm./100 gm. fresh weight)	Flesh (mgm./100 gm. fresh weight)
Pineapple orange	172	52
Marsh grapefruit	233	87
Dancy tangerine	206	27
Corregia lemon	161	18
Persian lime	209	146

Amounts of quinic acid present in the peel and flesh of mature fruit of several citrus varieties are given in Table 1. The quinic acid was determined by titration after elution from the column and complete removal of the acetic acid[7]. Results for the proportions of quinic acid relative to the other organic acids in citrus fruits will be published in due course.

This work was carried out in co-operation with the Florida Citrus Commission, Lakeland, Florida.

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BIOLOGY

Old and New Solutions to the Eel Problem

THE ingenious hypothesis proposed by Dr. D. W. Tucker[1] to explain the complex problems of the biology of the European eel presents in my opinion some heavy difficulties. I believe it therefore necessary to offer some observations with the intention of clarifying the question.

(1) When the European eel descends to the sea as a silver eel it does not show "a profound degeneration of the gut". The occlusion of the vent observed by Schnakenbeck[2] is, according to my experience, an entirely exceptional occurrence. All the silver eels I have examined had a gut of normal structure, although small in volume[3]. Silver eels kept in aquaria are indeed able to take up food again, although they are not so voracious as the yellow eels.

Survival and re-feeding of silver eels is not followed by regression of the gonads. Regressive pictures are frequently observed in the eels' gonads, even in the yellow eels ; but this is a cytological phenomenon that does not affect the whole gonad as an organ[4].

The whole organization of the descending eel does not present any indication of nearing death. Changes in colour and structure of the teguments, eye enlargement, transformation of retinal pigments[5], functional activation of the endocrine system are all conditions suggesting that when silver eels are going to live in deep marine waters they are still endowed with an intense vitality.

(2) On the basis of Schmidt's[6] results, it seems that European and American eels spawn in two slightly displaced areas ; but we cannot exclude the possibility that these areas are coincident. In any event there is no evidence sufficient to support the idea that a temperature difference of a few degrees would be enough to induce two sets of genetically homogeneous larvæ to acquire such different numbers of myomeres as 103–111 (average 107·2) for *Anguilla rostrata* and 110–119 (average 114·7) for *A. anguilla*. Even in the youngest larvæ or prelarvæ, there are clearly discrete myomere numbers[7], and to admit such a strong environmental influence would require the assumption that the eggs, from the beginning of their development, are separated into two completely isolated groups, one of which is carried in warmer, the other in cooler waters, without intermediate conditions. Hydrographic hypotheses do not seem to be sufficiently well founded to explain such a clear-cut separation of two variability curves of the myomere numbers as observed by Schmidt[7] between the larvæ of the American and the European eel.

The differentiation in the myomere numbers occurs in any event too early to be related to the influence of the Atlantic currents with their different temperatures. In the spawning area there are no sharp limits between cold and warm superficial waters, but a gradual variation from south to north of only 4 deg. C.

It is true that there are still a number of difficulties in explaining the life-history of the eel. It is particularly difficult to prove that all the Mediterranean eels are compelled to go out to the Atlantic. However, the fact that we are not able to capture them in the Strait of Gibraltar is not decisive evidence against such a migration.

The biology of the eel is certainly one of the most puzzling problems in marine biology, but the interpretation proposed by Dr. Tucker requires so many new hypotheses that it is too difficult to accept it on the basis of present knowledge.

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Prof. D'Ancona's objections are mainly due to misunderstanding and are met by my original paper[1], where not directly by a necessarily condensed text, implicitly through the literature cited.

(1) His divergent assessment of the silver eel depends upon his experience being confined to eels in the early stages of transformation. Schnakenbeck[2] and Berndt[3] have described autolysis and phagocytosis of the gut tissue by tissue, while Bertin[4] concludes his readily available (and illustrated) summary of their work by remarking: "Such, broadly, is the state of dilapidation to which the digestive tubes of the silver eel are reduced".

The occlusion of the vent reported by Schnakenbeck[2] in a North Sea specimen was not represented as other than a unique observation. But the condition of this eel, with its normal genital papilla, has been accepted as a typical and non-pathological continuation of a process the later stages of which are generally concealed from our study and is to be taken as representing the state attained in European continental waters by eels which survive thus far.

My remarks concerning regression of the gonad were intended to refer to cytological, physiological and metabolic phenomena rather than to gross morphology.

The whole point of my comparative discussion of the American and European migratory eels was that the advanced modifications of the European eel appear to be ill-adapted to the time-table of a presumed return journey. We may indeed know that a motorist is in the best of health but, as we watch him driving down a mountain road, intoxicated and without brakes, we can still legitimately say that his celebration was premature and that he is unlikely to reach his destination.

(2) Here I must ask Prof. D'Ancona to re-read my original paper. I did, in fact, suggest that the temperature conditions over the spawning-area of the eels admitted of the possibility of environmental determination of the somite-numbers; the suggestion stands as a hypothesis, not as an alleged fact or dogma, and its further treatment appears to be a matter for observation and experiment rather than for mere expressions of opinion. Prof. D'Ancona's remark about the "gradual variation . . . of only 4 deg. C." confirms my belief that he has not appreciated the four-dimensional nature of my argument.

I cannot agree that my interpretation requires the admission of many new hypotheses. It requires, admittedly, that a great deal of evidence which we have been accustomed to viewing in one familiar pattern must now be re-arranged into a drastically new one. But, as I showed in a comparison of Schmidt's ideas and my own, I make only one unfounded assumption: that the eel somite-numbers may be affected by temperature in the same way as those of numerous other fishes. The basic idea, once grasped, is so simple that anticipation was a constant fear while the paper was in preparation. Whether it is ingenious, or merely ingenuous, must, in the absence of any more convincing citation of available evidence, be a matter now for research rather than for philosophical speculation.

Two further points may be mentioned which have recently come to hand. First, Carlisle and Denton[5] have shown that in the metamorphosis of the visual pigments, as in several other characters already discussed[1], the European silver eel is more advanced than the American eel. Secondly, Dr. Winifred E. Frost has kindly brought to my attention a paper[6] on the age and length of the American eel.

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Number of Fibres in the Optic Nerve and the Number of Ganglion Cells in the Retina of Anurans

Using a light microscope, Bruesh and Arey[1] found that there were about 15,300 myelinated and 13,700 unmyelinated fibres in the optic nerve of the frog (*Rana pipiens*), and about 10,200 myelinated and 5,500 unmyelinated fibres in the optic nerve of the toad (*Bufo americanus*). However, in my electron microscope study of the optic nerve of these and other Anurans (*Rana catesbeiana*, *Bufo terrestris* and *Hyla cinerea*) I have found[2] that the unmedullated axons are in a considerably larger number, having been underestimated by a factor of 30 or more, and that most of them could not have been resolved with the light microscope. My observations, though, do not greatly contradict the earlier numbers of myelinated fibres, for these can be counted with reasonable accuracy after myelin stain. In the present communication I only wish to report about the general arrangement of the unmyelinated axons and their number. The full description of the fine anatomy of the optic nerve is deferred to an extensive article now in preparation.

Optic nerves were fixed in buffered (*p*H 7·4) osmium tetroxide and embedded in methacrylate. In all species studied, the unmyelinated axons are 0·15–0·6μ in diameter, and under the electron microscope appear in bundles of many closely packed axons, surrounded by glial cell expansions and myelinated fibres (Fig. 1). No glial cell intrudes between the unmyelinated axons of a bundle, and they remain separated from each other only by a gap of extracellular space 100–200 A. wide; a similar gap separates the unmyelinated axons from the surrounding glia or adjacent myelinated fibres. This space is continuous with that between the glial membranes which form mesaxons. Due to such close packing, the unmyelinated fibres cannot be adequately resolved with the light microscope, for while most of the unmedullated axons are within the limits of resolution of this instrument, the distances which separate them are very much less.

Both under light and electron microscopy, myelinated and unmyelinated fibres appear (in the gross) uniformly distributed across the nerve, with no sign of regional differences in density of one or the other. In these circumstances the number of unmyelinated axons can be calculated by multiplying the ratio of unmyelinated to myelinated fibres by the number of medullated axons counted in myelin-stained material. Random sampling in a cross-section of a nerve gave a ratio of 31/1 (*S.E.* = 3) unmyelinated to myelinated axons in the frog (*Rana pipiens*). The different field samples varied between ratios of 21/1 and 57/1; a total of about 4,000 fibres were thus counted in fifteen fields. A similar procedure gave a ratio of

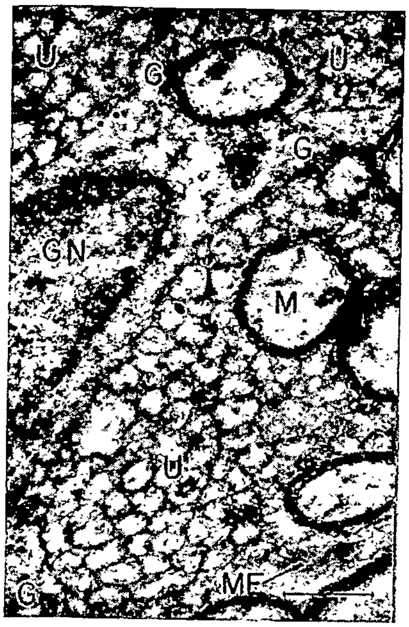

Fig. 1. Electron micrograph of a transverse section of the optic nerve (*Rana catesbeiana*). Fixation with buffered (*p*H 7·4) osmium tetroxide and methacrylate embedding. Notice the closed circular profiles which correspond to transverse sections of unmyelinated axons (*U*). Notice their relations with neighbouring glial cells (*G*) and myelinated fibres (*M*). *GN*, glial nucleus; *ME*, mesaxon. Scale 1μ

about 30/1 (*S.E.* = 3) unmyelinated to myelinated fibres in the toad (*Bufo americanus*), with ratios which varied from 15/1 to 53/1 in the different fields. About three thousand axons were counted in twelve fields. Using Bruesh and Arey's counts of medullated fibres, there would appear to be about 470,000 unmyelinated axons in the frog, and about 320,000 in the toad.

By means of degeneration experiments it can be shown that most of, if not all, the non-medullated axons are of retinal origin. Simply on the basis of numbers they must arise for the most part from ganglion cells 7–10μ in diameter present in the retina. Due to their small size, cells like these have been usually considered as glia[3]; but that they really are ganglion cells can be shown in retinas stained with methylene blue. There the axons and dendrites are revealed. Counts in three eyes of *Rana pipiens* show about 440,000 of these small ganglion cells in each retina. Larger ganglion cells, mostly 14–20μ in body diameter, number about 12,000; they most probably give rise to the larger myelinated axons. In any event, the partition of small and large ganglion cells in the retina follows that of myelinated and unmyelinated axons in the nerve. In these counts I used the Abercrombie[4] method for counting nuclei in microtome sections; 10 per cent of the total population of ganglion cells was actually counted. The discrepancy in the number of axons in the nerve and ganglion cells in the retina is at least partly due to the presence of myelinated efferent fibres[5], and may also be due partly to the existence of unmyelinated efferent axons.

The results presented here show that nerve fibres in the optic nerve of Anurans cannot be accurately counted under the light microscope, and that electron microscopy is required to reveal fully the unmyelinated axons. A similar revision may be needed in the estimates of fibres and retinal ganglion cells in the visual system of other vertebrates.

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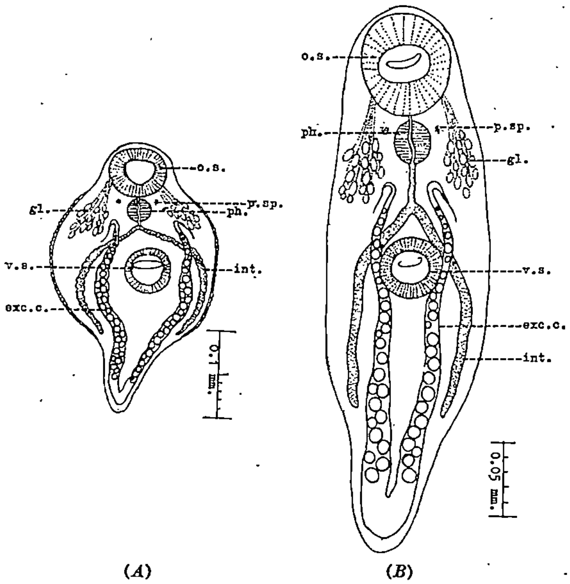
Metacercaria (Allocreadioidea) in the Planktonic Ctenophore, *Pleurobrachia globosa* Moser 1903, from the Madras Coast

Various marine invertebrates have been known to harbour cercariæ or metacercariæ of trematodes of fishes. Late cercariæ of *Opechona* (=*Pharyngora*) *bacillaris* were found in medusæ of *Obelia* sp., *Cosmetira pilosella*, *Turris pileata* and *Phialidium hemisphericum*, as well as in the ctenophore *Pleurobrachia pileus*, by Lebour[1] at Plymouth, and by Stunkard[2] (from the ctenophore only) at Roscoff, Finisterre. After a long interval, Franc[3] described the same metacercaria from *Phialidium hemisphericum* and *Pleurobrachia pileus* in France. There appears to be no other report of larval trematodes from ctenophores, although many other marine invertebrates, such as medusæ, siphonophores, copepods and chætognaths, have been described as their natural hosts by Poche[4], Martin[5], Dollfus, Anantaraman and Nair[6], and Dawes[7].

In the present communication, metacercariæ are reported from *Pleurobrachia globosa* collected from Madras inshore plankton. The rate of infection was 1–3 parasites in each of 8 of the 14 ctenophores examined. They were in an un-encysted condition and moved actively with the aid of the suckers when liberated from the gastric cavity of the hosts. Camera lucida drawings of a specimen in a contracted and an extended state were made (Fig. 1*A* and *B*).



(*A*) (*B*)

Fig. 1. Metacercaria from *Pleurobrachia globosa*: *A*, contracted; *B*, extended. Key: *exc.c.*, excretory canal; *gl.*, glands; *int.*, intestine; *o.s.*, oral sucker; *ph.*, pharynx; *p.sp.*, pigment spot; *v.s.*, ventral sucker

The larva is identified as a metacercaria, as it has no caudal appendage and reflects the adult condition except for the genitalia. The body is elongate, 0·390 mm. × 0·111 mm., broader in the anterior region, and covered with a thick non-spinous cuticle. The oral sucker is conspicuous and large, 0·058 mm. in diameter. The mouth leads to a muscular pharynx, 0·039 mm. × 0·020 mm., situated immediately behind the oral sucker, a pre-pharynx being practically absent. The short œsophagus bifurcates into the intestinal crura, which are broader than the œsophagus itself, and extend posteriorwards up to three-quarters of the length of the body. The ventral sucker is also circular, 0·039 mm. in diameter, and therefore smaller than the oral sucker. It is situated about the middle of the body behind the region where the œsophagus forks. Bundles of gland cells are present on the sides in the anterior region. There is a pair of faintly staining pigment spots, one on each side of the pharynx. The lateral excretory canals are very prominent, only slightly wavy, and are filled with large globules. They are continuous at the posterior end and open out through a short median stem. They become gradually narrower as they go forward and turn back in the œsophageal region. There is no distinct structure as an excretory bladder, and the excretory system therefore appears as an extended V with an insignificant median duct.

This metacercaria needs to be compared with the only one known from a ctenophore, namely, that of the Allocreadiid *Opechona bacillaris* described by Lebour[1], Stunkard[2] and Franc[3]. It differs from it in having wide lateral excretory canals forming a V-shaped pattern, glandular structures associated with the oral sucker and no pre-pharynx. Assuming that this metacercaria is also derived from a trichocercous cercaria, it should be considered as belonging to the ocellate group of marine trichocercous cercariæ, classified by Dollfus[8] together with that of *Opechona bacillaris* and others enumerated by Dawes[9]. Its adult may therefore be a trematode similar to the genus *Opechona* and parasitic in fish hosts which ingest ctenophores.

La Rue[10] has formulated a new system of classification of the Digenea on the basis of life-cycle patterns and larval morphology, providing a key to all the families. This approach will be of immense value in identifying larval trematodes the adults of which have not been related to them, and in solving the life-cycles of many of them. The present metacercaria falls under the super-family Allocreadioidea Nicoll 1934, as an ophthalmotrichocercous kind, and may belong to one of the seven families listed under it, namely, Acanthocolpidae Luhe 1909, Allocreadiidae Stossich 1903, Lepocreadiidae Nicoll 1934, Megaperidae Manter 1934, Monorchidae Odhner 1911, Opecoelidae Ozaki 1925 and Opistholebitidae Fukui 1929—most probably Allocreadiidae. Three hosts are usually involved in the life-cycle of the representatives of these families, and in the present case they could be the gastropod (or lamellibranch), the ctenophore (or medusa, copepod, or *Sagitta*), and the fish.

Pelagic organisms serve as food for marine vertebrates and should accordingly be expected to carry the larval stages of helminths developing to maturity in the latter. The examination of other representatives of the planktonic biota in the coast of Madras is being continued in the hope of discovering more of these larval helminths.

I gratefully acknowledge the guidance of Prof. C. P. Gnanamuthu in this investigation, which was begun during the tenure of a Government of India senior scholarship.

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An Albino Specimen of the Common Frog

ON February 22, Mr. L. Gentry, of Blacksmith Hill, Sanderstead, Surrey, found an albino specimen of the common frog (*Rana temporaria*) in his garden. He presented the frog to this Museum, and it is now living in the Aquarium.

The frog is a male with the back and legs an evenly coloured yellow and the ventral surface a whiter tone. The thumb pads are a dark brown and the eyes a bright red.

It is hoped that this frog will breed with normal females, and various workers have agreed to hatch the spawn and rear the frogs with the view of trying to establish an albino strain.

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Influence of Temperature on the Number of Vertebræ in Fish

THE number of vertebræ in fish is considered to vary with temperature during early development. From field observations, it is generally considered that fish subjected to low temperature tend to have more vertebræ than those in warmer waters. This was supported by the experiments of Gabriel[1] on *Fundulus heteroclitus*, of Dannevig[2] on *Pleuronectes platessa*, and of Kubo and Kobayashi[3] on *Oncorhynchus keta*. On the other hand, Tåning[4] showed that the lowest average number of vertebræ was obtained at an intermediate temperature, while both higher and lower temperatures produced a higher average in his experiment on *Salmo trutta trutta*. A similar result was obtained by Lindsey's[5] experiments on *Macropodus opercularis*. Thus the results of experimental studies are not consistent.

I reared eggs at different constant temperatures throughout the sensitive period from one pair of snake-head fish *Channa argus* (Cantor), and examined the vertebral number of the young fish of each group. The experiment was repeated three times using three different pairs. The results are given in Table 1.

From the results, it may be concluded that: an intermediate temperature produces a lower average number of vertebræ than either high or low temperature in *Channa argus*; genetic factors seem to have more effect on the number of vertebræ than environmental ones. The first conclusion does not coincide with the generally accepted view mentioned above, but coincides with the results of Tåning's and Lindsey's experiments.

Table 1. Distribution of Vertebral Numbers in *Channa argus* Raised at Different Constant Temperatures

Experiment	Raised at (° C.)	Number of vertebræ							Total number of fish examined	Average number of vertebræ	P
		56	57	58	59	60	61	62			
1	29·5	5	247	372	21				645	57·63	$P < 0·001$
	22·5	11	222	208	13				454	57·49	$P < 0·001$
	19·5–22·5*	4	144	266	48				462	57·77	
2	29·5	1	15	64	5				85	57·86	$0·3 < P < 0·5$
	26·1†	2	1	11	1				15	57·73	$P < 0·001$
	25·0	4	44	8					56	57·07	$P < 0·001$
	22·5	2	40	83	2				127	57·67	$0·5 < P < 0·7$
	20·0	10	50	125	17				202	57·74	$0·001 < P < 0·01$
	19·5	4	19	61	22				106	57·95	
3	29·0		5	309	741	87	4		1,146	58·80	$P < 0·001$
	25·0		35	559	332	5			931	58·33	$P < 0·001$
	22·5		1	16	294	198	7	2	518	59·39	

* This group was raised at 19·5° C. during the embryonic stage and then was transferred to 22·5° C.

† This group was raised in an ordinary room the temperature of which was not controlled. The average temperature of the room during the sensitive period was 26·1° C.

Details of this work will be published in the *Bulletin of the Japanese Society of Scientific Fisheries*. I am grateful to Prof. Tamotsu Tamura for his advice.

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Vibrio spp. in Finnock from the Aberdeenshire Dee

In August 1958 reports of dead finnock (young sea trout) were received from the fishermen operating sweep nets near the mouth of the River Dee. These fish were reported either to look quite healthy or to have some hæmorrhagic marks on the belly. A number of these fish were examined and the same organism was isolated, from all, in almost pure culture, on both nutrient agar and a sea-water agar. This organism has now been studied morphologically and biochemically and the results obtained indicate that it is a species of *Vibrio*.

Finnock from another river where there had been no noticeable mortality were inoculated with this organism. When the inoculation was intraperitoneal the fish died within six days when kept in fresh water. They showed no outward sign of disease, but yielded pure cultures of the organism from all the organs.

With subcutaneous inoculation the fish again died, within 48 hr., and the muscle around the site of the inoculation became hæmorrhagic, as in the specimens from the Dee, although this hæmorrhagic area did not show through the skin. Again pure cultures of the organism were obtained from the organs and the muscle. Although uninoculated finnock from the same source kept in fresh-water for four days and then in 50 per cent sea water for four days (to eliminate fungus) died due to a failure of the air supply, none of these yielded the *Vibrio*. The organism was found to grow more vigorously in sea-water media, so these fish can be considered as the controls.

A similar outbreak appears to have occurred in the Dee in 1957 when, unfortunately, only one fish was received for examination from a number reported dead. Similar organisms were isolated from this fish as also from an isolated finnock found dead in the Dee in 1954.

These outbreaks among finnock seem to be similar to those reported by Hoshina[1] in rainbow trout in Japan, where the infection was attributed to *V. piscium* var. *japonicus*. The latter is similar to the organism isolated from finnock. This disease may also occur in marine fish as Hotchkiss (personal communication) has found a similar organism which caused the death of many saithe near Shetland in 1949. The fact that *Vibrio* can infect both fresh-water and salt-water species is borne out by a summary of *Vibrio* species infections published recently by Rucker[2].

A fuller account of these investigations will be published elsewhere.

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Marginal Growth of Leaves

Recently the marginal meristem of foliage leaves has been discussed by Pray[1] for monocotyledons and by me[2] for dicotyledons.

In dicotyledonous foliage leaves marginal and submarginal types of marginal growth can be recognized depending on the origin of the procambium[2]. The latter type may be subdivided into the adaxial (Fig. 1*D*), abaxial (Fig. 1*E*) and middle (Fig. 1*F*) types. In certain instances an intermediate condition between two types has been observed[3]. Except for some variegated leaves[4,5], *Daphne odora* is the only dicotyledon showing the marginal type of growth in its foliage leaves[2,6], development proceeding according to the pattern shown in Fig. 1*C*. Recent observations indicate that *Daphne pseudo-mezereum*

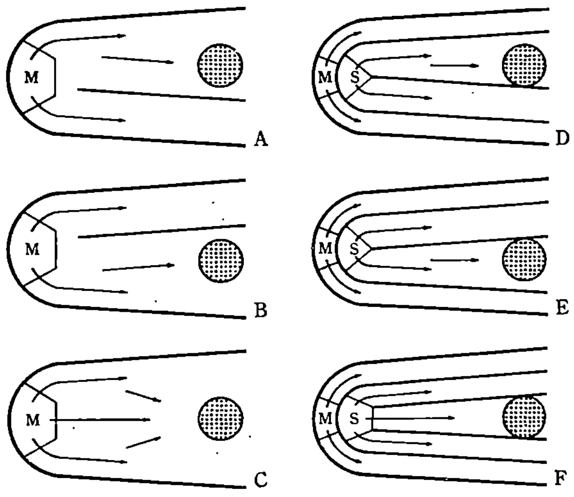

Fig. 1. Diagrams showing variations in activity of the marginal meristem of the leaf. The adaxial side is shown in the upper side of the figure. Stippled part is the procambium. *A–C*, marginal type; *D–F*, submarginal type *M*, marginal initial; *S*, submarginal initial

also shows a marginal type of development but follows the pattern shown in Fig. 1*A*.

I considered that the types of development recognized for dicotyledonous foliage leaves could also be applied to other categories such as scale leaves and monocotyledonous leaves which show marginal growth[3]. Observations of the scale leaf of *Rhododendron nipponicum* showed the marginal type of growth indicated in Fig. 1*A*. Foster[7] also reported the marginal type of development in the scale leaf of *Rhododendron*. Pray[1] did not see evidence of active periclinal divisions of marginal initials or protodermal cells in the leaf of *Philodendron*, which is classified as the type shown in Fig. 1*E*. However, Pray did find possible evidence of a periclinal division of a marginal initial, suggesting that this instance might possibly be classified as the type shown in Fig. 1*B*. Pray also described leaf development in *Hosta* where the pattern was that illustrated in Fig. 1*C*.

Thus, the subdivisions recognized in the submarginal type (Fig. 1*D–F*) may also be recognized in the marginal type (Fig. 1*A–C*). In many instances a fixed and unchangeable type of marginal growth during leaf development cannot be recognized in individual species; but it would appear that the type of marginal growth is diagnostic for each species if characteristic fluctuations in the ontogenetic process in general are considered.

I investigated phylogenetic correlations between the various types of marginal growth in one group—the Ericaceae and their allies[3]. Recently, however, variations in marginal growth have been reported for dicotyledons, monocotyledons and gymnosperms[1-3,8-10]. Interpretations of the relationships between the types in these groups will depend on more comprehensive investigations, both ontogenetically and phylogenetically, in seed plants or in vascular plants in general, including the ferns. The relationship between the marginal and submarginal types is particularly interesting. There may be direct correlations between the patterns seen in Fig. 1*A* and *D*, *B* and *E* and *C* and *F*. Possible evidence of this relationship is seen in *Rhododendron*. The scale leaf of *R. nipponicum* follows the pattern shown in Fig. 1*A* in its development; but other species of *Rhododendron* examined by me, and the Ericaceae in general, follow the pattern in Fig. 1*D*. Also the leaf of *Philodendron* suggests a pattern which is interpreted as being intermediate between that shown in Fig. 1*B* and that in Fig. 1*E*.

I wish to acknowledge my indebtedness to Dr. B. F. Palser, University of Chicago, for kindly going through this manuscript.

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Regulation of Morphogenesis in an Oleaceous Tree, *Nyctanthes arbor-tristis*

The pioneers of biometry published many figures on the variation in flowers of numbers of petals, sepals, stigmatic bands, and so on. As they worked on herbs, they counted small numbers, and though they found differences in the means of different plants, were unable to compare the variances, either between plants or between the same plant at different times. *Nyctanthes arbor-tristis* Linn. (Oleaceae) sheds up to 1,492 flowers nightly, and up to 32,790 in a season, normally from September to early January in Calcutta.

Three trees of this species were observed throughout the season 1955–56 (ref. 1), and seventeen for seven weeks in 1957. Table 1 gives the grand total.

Table 1. Overall Frequency Distribution of Flowers (for Three Trees in 1955–56 and Seventeen Trees in 1957) according to Number of Petals

No. of petals	4	5	6	7	8	9	15	Total
No. of flowers	451	29,147	109,345	18,956	1,012	14	1	158,926

It will be seen that most flowers (68·8 per cent) had six petals. In 1957 the means for the seventeen trees ranged from 5·50 ± 0·0081 to 6·27 ± 0·0088. Most means differed significantly from all others. The means for three trees measured in successive years were 5·92, 5·89; 6·05, 6·09; and 5·98, 6·01. The differences were significant but small.

Fig. 1 shows the changes in the means for three trees during a season. In order to obtain a moderately smooth graph I took moving means over five consecutive days. It will be seen that for each tree the mean fell and then rose again.

The standard deviations also differed in the different trees, ranging from 0·5108 ± 0·0052 to 0·6605 ± 0·0069. Again many differences were highly significant. As, however, the usual test of significance for the difference of two variances is only valid when the distributions are normal, and the fourth moments are not very well determined, I tested the percentages of abnormality, that is to say, the percentages of flowers with a number of petals other than six. These often differed very significantly even when the means did not. The standard deviations increased systematically through a season as shown in Fig. 2, though for one of the trees they dropped on two occasions. The changes in means and standard

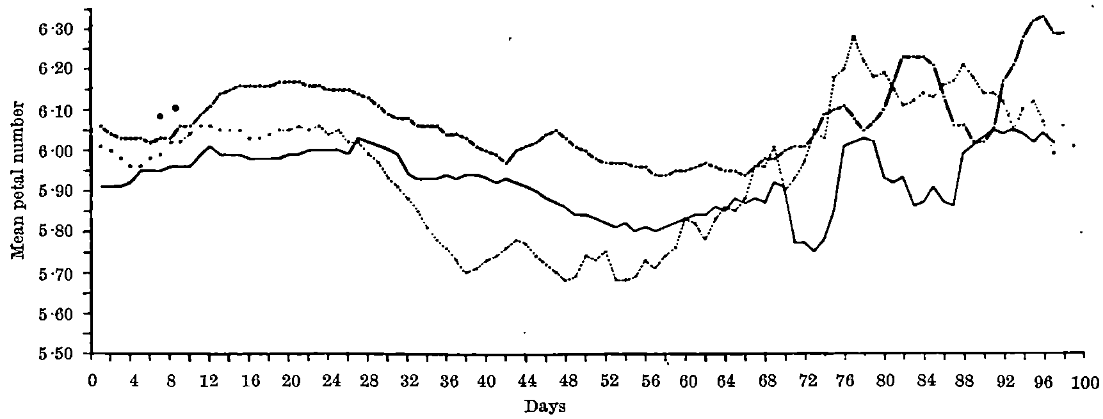

Fig. 1. Moving means of petal numbers over five consecutive days for three trees during the season 1955–56. ———, Tree No. 1; —·—·, tree No. 2; ...., tree No. 3

deviations alike are about 0·1–0·2. The point is that the means changed by about 2–4 per cent, and the standard deviations by 20–40 per cent or so.

If a craftsman produced articles with much the same mean dimensions in the course of a day's work, but their variance around this mean increased progressively, we should say that he was getting fatigued. It might be possible to trace this fatigue to a decline in the efficiency of 'negative feedback'. It is not so easy to apply this notion to a plant. The weather became progressively cooler during the flowering season, and the increased variance might be ascribed to this. However, I have observed the same increase in variance of petal number during the flowering season in two plants of each of *Jasminum pubescens* var. *alba* and *Jasminum pubescens* var. *rubescens*, although in these cases the temperature was rising. The closest analogy known to me is the case of pernicious anæmia in man. Here Price-Jones[2] showed that the mean diameters of red blood corpuscle increased moderately, but the standard deviation increased much more. Such words as regulation and homœostasis are applied to the processes by which such variables as body-temperature and blood glucose-level are kept relatively steady. Here we can measure the efficiency of regulation by the reciprocal of the variance in a set of successive values, and the regulation can be shown to depend on a negative feedback system. It may not be so easy to apply this notion to the standardization of a set of simultaneous performances.

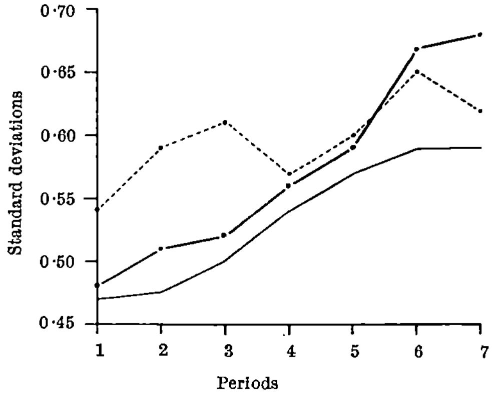

Fig. 2. Standard deviations for seven consecutive periods of sixteen days each for three trees during the season 1955–56 ———, Tree No. 1; ·—·—·, tree No. 2; ·--·--·, tree No. 3

Whatever the nature of the regulatory process, its efficiency can be measured. I suggest that the variance of a metrical character may be as important a property of an organism as its mean, and should be measured on a number of species. This is being done at this Institute, but I hope that similar work may be undertaken outside India. A detailed account of the work described here will be published elsewhere.

I wish to thank Prof. J. B. S. Haldane for help both with the practical and theoretical investigations.

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BACTERIOLOGY

Reclassification of *Leuconostoc mesenteroides* P.60 as a *Pediococcus*

FOR some time it has been known that the organism widely used for the assay of amino-acids and called *Leuconostoc mesenteroides* *P*.60 is not in fact a *Leuconostoc*. McCleskey[1] examined *P*.60 and suggested that it might be *Streptococcus equinus*. However, the culture was atypical mainly because it produced ammonia and carbon dioxide from peptone. McCleskey suggested that the culture should be known as *Streptococcus* spp.

A strain of *P*.60 obtained from the National Collection of Industrial Bacteria, at Teddington, *NCIB* 8081, has been examined and found to have many features in common with *ATCC* 8081, and other strains of *Pediococcus cerevisiae*[2]. The comparison is given in Table 1.

Pediococci have only recently become recognized as a widely distributed genus, mainly because of the difficulty in separating them from other genera. However, *P*.60 possesses the essential characters of a *Pediococcus*. Morphologically it is a Gram-positive coccus occurring in pairs and tetrads, and can be separated from the morphologically similar aerobic Micrococcaceae by the type of growth produced on agar and because carbohydrate is required for growth. Unless catalase is demonstrated to be present in the *Pediococci*, the distinction between the *Streptococci*

Table 1. A COMPARISON OF *Pediococcus cerevisiae ATCC* 8081 AND *Pediococcus* (*Leuconostoc mesenteroides*) *P*.60

Similarities

Morphology	Gram + coccus in pairs and tetrads
Type of growth on yeast glucose agar	Small round unpigmented colonies similar to those produced by streptococci
Growth on nutrient agar	Very slight
Litmus milk	–
Hydrolysis of arginine	+
Growth at *p*H 9	–
Growth at *p*H 4·8	+
Acid produced from	Arabinose, fructose, glucose, galactose, mannose, cellobiose, trehalose, salicin, aesculin
No acid from	lactose, sucrose, dextrin, mannitol

Dissimilarities

		ATCC 8081	*P*.60
Catalase		+	–
Folinic acid		required	not required
Acid from :	xylose	–	+
	maltose	+	–
	glycerol	+	–

and the *Pediococci* rests on morphology. Gutekunst *et al.*[3] have shown that the production of catalase in the *Pediococci* may depend on the conditions of growth, and even when present may be difficult to demonstrate. *P*.60 has not been shown to produce catalase, and hence the confusion with the *Streptococci*. The lack of catalase does not exclude the culture from the genus *Pediococcus*.

Felton and Niven[4] examined several strains of *Pediococcus cerevisiae* and found that they all required folinic acid for growth, and they suggested that the need for folinic acid might be a "unique characteristic" required by the genus as a whole. Günther[5] has found that five out of thirteen strains belonging to *Pediococcus cerevisiae* do not require folinic acid.

It was intended to compare *P*.60 with authentic strains of *Streptococcus equinus* ; but attempts to obtain these cultures from world sources resulted in three cultures being received, each one different from the other. However, several other strains of *Pediococcus cerevisiae* have been examined, and it is now concluded that *P*.60 belongs to the same genus, and is not a *Streptococcus*. Günther[5] has confirmed the observations, and has placed *P*.60 with her group *I*, that is, *Pediococcus cerevisiae*.

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Uronate Oxidation by Phytopathogenic Pseudomonads

THE pathway by which D-galacturonic and D-glucuronic acids are utilized by phytopathogenic *Pseudomonas* species is apparently quite different from the uronic isomerase–keturonic reductase system found in three genera of the Enterobacteriaceae[1–5]. In this new pathway of uronic acid catabolism, mucic acid has been isolated and identified as the initial product following the enzymatic oxidation of D-galacturonic acid; glucaric acid is presumably formed from D-glucuronic acid.

Cell-free extracts prepared from galacturonate- or glucuronate-grown *Pseudomonas syringae* and other phytopathogenic pseudomonads contain an enzyme which catalyses the rapid oxidation of either D-galacturonate or D-glucuronate with DPN+ but not TPN+. This enzyme, named uronic acid dehydrogenase, has been purified several-fold by ammonium sulphate precipitation, followed by *DEAE* cellulose column chromatography. Failure to find separate dehydrogenases, or to show differential activity upon either substrate during the several steps of purification, suggests that the same enzyme may catalyse the oxidation of both uronates. The purified enzyme does not act upon glucose, galactose, L-iduronate, or D-mannuronate, with either DPN+ or TPN+. Uronic dehydrogenase activity was found in extracts prepared from mucate- and glucarate-grown cells, but no detectable quantity of this enzyme was evident in extracts prepared from cells grown with glucose. Neither uronic isomerase nor keturonic reductase activity was detected in preparations from uronate-grown *P. syringae*.

The end-products formed upon the enzymatic oxidation of either D-galacturonate or D-glucuronate are non-reducing, lactonizing acids. Several mgm. of the oxidation product formed from D-galacturonate were prepared by coupling the *Pseudomonas* system with *Azotobacter*-reduced diphosphopyridine nucleotide-oxidase and oxygen. After deproteinizing and condensing the reaction mixture, a very insoluble white crystalline precipitate was obtained. Upon recrystallization from hot water, this substance had a melting point identical with that of authentic mucic acid ; no depression of melting point was observed when the two compounds were mixed.

The stoichiometric picture supports our belief that *P. syringae* converts galacturonate plus DPN+ to mucate plus reduced diphosphopyridine nucleotide ; 0·238 µmole of the latter appeared in a system originally containing 0·236 µmole galacturonate (Fig. 1). Furthermore, whole cells of galacturonate-grown, but not glucose-grown, *P. syringae* are sequentially induced to the oxidation of mucate.

Enzymatic attack on glucuronate similarly yields an equimolar quantity of reduced diphosphopyridine nucleotide (0·215 µmole from 0·214 µmole glucuronate ; Fig. 1). Glucuronate-grown, but not glucose-grown, whole cells are simultaneously adapted to the oxidation of glucaric acid. Unequivocal identification of the end-product, presumably glucaric acid, is at present under investigation, as are the steps beyond the sugar dicarboxylic acids in this new pathway of uronic acid metabolism.

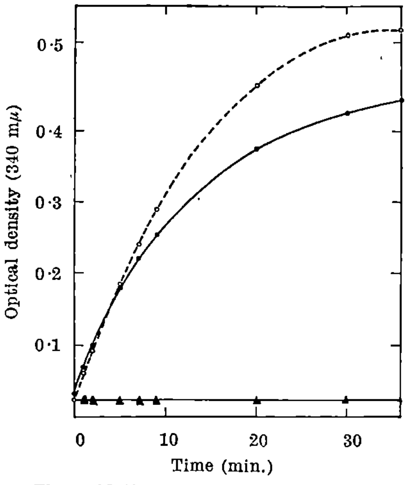

Fig. 1. The oxidation of D-galacturonate and D-glucuronate with DPN+ and purified uronic acid dehydrogenase from *Pseudomonas syringae*. Cuvette contents were : substrate (○—○, 0·236 µmole galacturonate ; ●—●, 0·214 µmole glucuronate ; ▲—▲, none) ; 100 µmoles *tris*-hydrogen chloride buffer, *p*H 7·4 ; 0·6 µmole DPN+ ; and 0·1 ml. enzyme ; final volume, 3·0 ml.

This work was supported in part by Research Grant E-1067 from the U.S. Public Health Service, National Institutes of Health.

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Oxidation of Thiosulphate by *Thiobacillus thioparus*

PREVIOUS investigations of the oxidation of thiosulphate by the autotrophic micro-organism *Thiobacillus thioparus* have not led to uniform results. According to Starkey[1], thiosulphate is oxidized directly to sulphur and sulphate, and Parker and Prisk[2] have also come to a similar conclusion. On the other hand, Vishniac claims that the oxidation of thiosulphate by *Th. thioparus* occurs in two stages: the first is the complete oxidation of the substrate to tetrathionate and the second the oxidation of the tetrathionate[3]. The results of Pratt's investigations[4] also suggest the possibility of the appearance of tetrathionate during the oxidation of thiosulphate by *Th. thioparus*. Pratt showed that in the medium in which *Th. thioparus* was growing there was an accumulation of some substance, presumably tetrathionate, giving a positive Folin–Ciocalteu reaction.

Our previous investigations, based on the application of thiosulphate labelled with radioactive sulphur[5], argue against the hypothesis which assumes tetrathionate to be an intermediate substance in the oxidation of thiosulphate by this micro-organism. The application of a very sensitive chromatographic method for the separation of inorganic sulphur compounds has now enabled us to collect some new facts contradicting Vishniac's hypothesis.

The strain of *Th. thioparus* which we have isolated corresponds in its biological and morphological characters to the micro-organism described by Natanson[6] and Starkey[1]. It was cultured in the medium previously described[7]. The centrifuged culture medium was subjected to chromatographic analysis, using Whatman No. 1 filter paper and solvent recommended by Stelmasźyńska[8] (acetone/*n*-butanol-I/water, 2 : 2 : 1). The chromatograms obtained were stained in darkness with 0·1 *N* silver nitrate and then washed in water, a solution of ammonia and water again.

In Fig. 1*a* is seen a chromatogram on which the distribution of thiosulphate and four polythionates is marked. Fig. 1*b* reproduces the chromatogram obtained from bacterial medium in which 50 per cent of the initial quantity of thiosulphate has been consumed. In this chromatogram only one spot corresponding to thiosulphate is visible. Similarly, the chromatograms of the medium taken after the consumption of 25 per cent of thiosulphate exhibited only a single spot corresponding to thiosulphate.

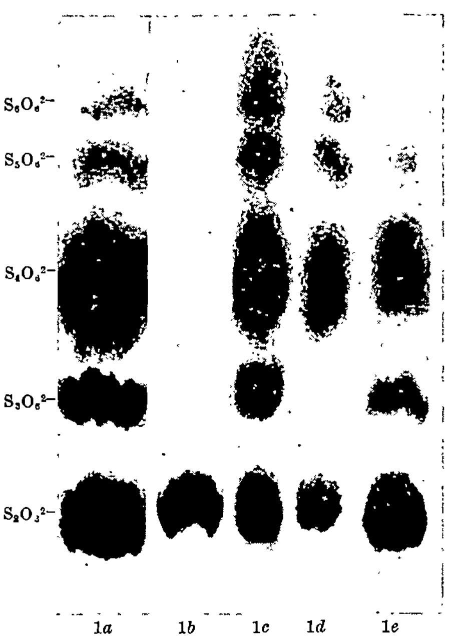

Fig. 1. Ascending chromatograms of thiosulphate and polythionate (*a*); of the reaction products between these substances (*c*, *d*, *e*); and of the medium in which *Th. thioparus* was cultured (*b*)

Our further experiments show that when tetrathionate appears in the solution besides thiosulphate, a series of spontaneous secondary reactions occur leading to the appearance of other polythionates. A mixture of equimolar (0·25 *M*) solutions of thiosulphate and tetrathionate, when subjected to chromatographic analysis, shows spots corresponding to trithionate, tetrathionate, pentathionate, hexathionate and probably heptathionate (Fig. 1*c*). If solutions of thiosulphate and tetrathionate are mixed with simultaneous addition of formaldehyde, there is an absence of trithionate in the products of the spontaneously proceeding reactions (Fig. 1*d*). We explain the appearance of polythionates under the conditions just described by the following reactions, the last of which is inhibited by formaldehyde:

$$^{-}S{-}SO_3^- + {}^{-}O_3S{-}S{-}S{-}SO_3^- \rightarrow {}^{-}O_3S{-}S{-}S{-}S{-}SO_3^- + SO_3^{=}$$

$$^{-}S{-}SO_3^- + {}^{-}O_3S{-}S{-}S{-}S{-}SO_3^- \rightarrow {}^{-}O_3S{-}S{-}S{-}S{-}S{-}SO_3^- + SO_3^{=}$$

$$SO_3^{=} + {}^{-}O_3S{-}S{-}S{-}SO_3^- \rightarrow {}^{-}O_3S{-}S{-}SO_3^- + {}^{-}S{-}SO_3^-$$

If, therefore, tetrathionate were to appear in the course of the oxidation of thiosulphate, we should expect to see, on the chromatograms of the medium, spots corresponding not only to this substrate but also to the other polythionates. As was previously stated, we have not seen this.

Of course, the objection may be raised that in the culture tetrathionate appears slowly, and that on account of this there occur conditions differing from those which arise after a rapid mixing of equimolar quantities of thiosulphate and tetrathionate. Wishing to decide this possibility, we carried out model experiments in which the tetrathionate solution was placed in a dialysing bag in a thiosulphate solution. The concentration of both solutions would finally correspond to that which would be found in the thiosulphate solution after the oxidation of 25 per cent of this substance to tetrathionate. Chromatographic analysis of the external and internal fluid taken after the experiment had lasted for 16 hr. at 32° C. showed distinct spots of thiosulphate, trithionate, tetrathionate and pentathionate (Fig. 1*e*). These results, in agreement with our former findings, lead to the conclusion that the oxidation of thiosulphate by *Th. thioparus* does not pass through the intermediate stage of tetrathionate.

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SOIL SCIENCE

Release of Fixed Ammonium from Soil by Ball Milling

RECENT research has shown that some soils have the ability to fix appreciable quantities of ammonium in a form not readily exchangeable with 1 *N* potassium chloride or available to plants and micro-organisms. Fixation results from a replacement by ammonium for interlayer cations (calcium, magnesium, sodium, hydrogen) in the expanded lattice of clay minerals. Since many soils contain the types of clay minerals known to fix ammonium, it may be deduced that they will contain fixed ammonium through the reaction of minerals with ammonium produced naturally. This deduction is supported by recent reports[1-4] that some soils contain considerable amounts of naturally occurring fixed ammonium. However, these findings require confirmation, since the methods employed cannot be considered entirely satisfactory.

The difficulty involved in the determination of native fixed ammonium in soil is that of finding a method that will secure quantitative release of fixed ammonium from clay minerals without causing decomposition of nitrogenous soil organic matter to ammonium. In the work reported here, the value of a method based on ball milling was investigated, since it was considered possible that grinding of soil under certain conditions might destroy the crystal lattices of clay minerals and release fixed ammonium without causing serious decomposition of organic nitrogen compounds. Studies were conducted with a clay mineral (vermiculite) and several soils. The vermiculite, which was previously saturated with ammonium and contained 9·6 mgm. of fixed ammonium nitrogen per gram, was ball milled both wet and dry. Steel jars and balls were used, since grinding of clay minerals with other types of jars or balls led to contamination of the minerals by abraded material. For wet ball milling, a 0·2-gm. sample was ground with 150 ml. of 1 *N* potassium chloride solution and 10 gm. of boric acid. Boric acid was added because preliminary experiments showed that ball milling of vermiculite and other clay minerals was accompanied by a marked rise in *p*H, which led to the loss of ammonium by volatilization. The ammonium released by grinding was determined by steam distillation of *N* potassium chloride extracts of the ball-milled materials, using a *p*H 8·8 borate buffer. The ammonia in the distillate was determined titrametrically, or colorimetrically with Nessler's reagent.

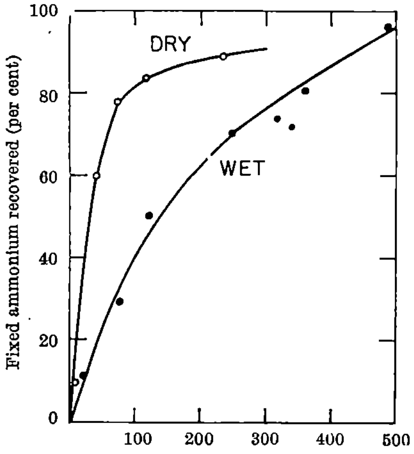

Fig. 1

The release of fixed ammonium in vermiculite to an exchangeable form as a function of time of ball milling is shown in Fig. 1. It can be seen that prolonged grinding was required to release the fixed ammonium and that quantitative recovery was not achieved. Dry ball milling was more effective than wet grinding, about 90 per cent of the fixed ammonium being released to an exchangeable form by dry ball milling for 230 hr. and by wet ball milling for 435 hr. Packing of unground material in the ends of the jar occurred in dry ball milling and this undoubtedly reduced the efficiency of grinding. Studies with a sample of vermiculite that had not been treated previously with ammonium showed that dry grinding for 290 hr. did not completely destroy its ammonium-fixing capacity, which indicates that either the crystal structure was not completely disrupted by grinding or that new types of ammonium-fixing minerals were formed.

The ball milling of several subsoils suspected of containing naturally occurring fixed ammonium led to a progressive increase in exchangeable ammonium with time of ball milling. For example, with a Cisne silt loam subsoil, 3·2 mgm. of nitrogen per 100 gm. was released by grinding for 48 hr., while 5·2 mgm. of nitrogen per 100 gm. was released by grinding for 120 hr. These results do not establish the presence of naturally occurring fixed ammonium in soil, since some of the ammonium released from the soil by ball milling could have come from the breakdown of soil organic matter. This possibility could not be tested directly, but experiments in which 1 gm. of clay-free peat soil was ball milled with 9 gm. of sand for periods up to 260 hr. showed that ammonia was produced in increasing amounts with increased periods of grinding. This finding must be interpreted with some caution, since the organic matter in peat soils may be more susceptible to decomposition by grinding than the material in mineral soils. Nevertheless, taken with the finding that quantitative release of fixed ammonium from vermiculite was not achieved even with long periods of grinding, this result indicates that methods based on ball milling are not likely to be of value for the determination of fixed ammonium in soil.

This communication is published with the approval of the Director of the Illinois Agricultural Experiment Station.

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Simultaneous Decomposition Processes in Soils

It has been found[1] that following the moistening of a dry soil two independent decomposition processes occur, namely, (1) decomposition of soluble organic material without nitrification and (2) decomposition of non-soluble organic material with nitrification. Both rates of decomposition fall off rapidly, with (1) as the soluble substrate is exhausted and with (2) as physical changes, among others, occur at the surface. These changes appear to involve organic gels the surface area of which is increased by drying, possibly as a result of fragmentation or increased porosity. On first moistening, a greater surface area is exposed to solution processes (followed by (1)), and to decomposition (2) than later when, under continued moist conditions, reversible changes occur in the colloids leading to reduced surface area. Prolongation of the dry state, without the soil necessarily becoming drier, increases the magnitude of (1) and (2), which indicates that ageing, a typical colloidal phenomenon, is involved. Moreover, since the behaviour described under (1) and (2) is repetitive with successive dryings and rewettings the changes in the colloids must be reversible, indicating that elastic gels are involved.

Further evidence for this two-process decomposition has recently been obtained. When a dry soil was moistened with water, and with normal solutions of sodium, potassium, calcium and magnesium chlorides and put in the respirometer for seven days the following amounts of carbon and nitrogen were mineralized (Table 1, stage 1).

Duplicate samples which had been through the same procedure as the above were then air-dried for 9 days, remoistened with water and again put in the respirator for a week. The amounts of carbon and nitrogen mineralized during this second cycle are given in Table 1 (stage 2).

A separate experiment (unpublished) showed that the salts depressed the solubility of the organic material and this is reflected in the greater amount of carbon mineralized in the water-treated sample, particularly during stage 1, which followed a long period during which the soil was in an air-dry state. There is, however, no indication that a reduction in the amount of carbon mineralized has had a concomitant effect in reducing nitrogen mineralization. If, as mentioned earlier, the two decomposition processes are independent, there is no reason why the repression of one should affect the other. This experiment therefore confirms previous experiments[1] in which it was found that when the soluble soil-organic material was extracted and added to both sand and soil media it decomposed without nitrification. Moreover, when the solution and decomposition of this soluble material is repressed, as in the above experiment, one gets a truer idea of the carbon/nitrogen ratio of the material actually involved in nitrification processes which, as shown in Table 1, is considerably less than the generally reported value of about 10, which usually includes carbon mineralized from both nitrifying and non-nitrifying processes.

Table 1
(Mgm./100 gm. soil)

Treatment	Stage 1			Stage 2		
	Carbon	Nitrogen	C/N	Carbon	Nitrogen	C/N
Water	19·8	1·95	10·2	10·2	0·90	11·3
Sodium chloride	10·2	1·18	8·6	9·6	1·85	5·2
Potassium chloride	9·6	1·64	5·6	7·2	0·84	8·6
Calcium chloride	8·4	1·73	4·9	9·0	1·80	5·0
Magnesium chloride	12·0	1·69	7·1	7·8	1·67	4·7

Nitrification, on moistening a soil, occurs initially under favourable conditions because the surface area exposed to decomposition and nitrification processes is greater soon after moistening than later on. Further, the newly developing microbial population is more active. The decomposition of microbial remains killed by drying must also be involved. This combination of circumstances leads to the subsequent production of considerable quantities of mineral nitrogen sometimes equivalent to that in 1 ton of sulphate of ammonia for an acre-6 in. of soil. The amount produced depends on the humus content of the soil and the logarithm of the time the soil was in an air-dry state prior to moistening. The decline in the rate of nitrification after moistening has been found to conform closely to a first-order reaction. Both the effect of drying on nitrification and the course that this afterwards follows can therefore now be fairly well predicted. This is important in relation not only to soil fertility but also to the effect of nitrate on other soil constituents. It may, for example, affect the solution of bases.

In conclusion, it is interesting to speculate on the wider application of the principle involved in the drying effect (par. 1). It seems that further use can be made of a colloidal system which is reversible with successive wettings and dryings and which exposes the maximum area to solution and decomposition processes for only a short period after each wetting.

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[1] Birch, H. F., *Plant and Soil* (in the press).

FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Tuesday, May 19

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Prof. M. E. L. Mallowan: "Ancient Mesopotamian Concepts of the Animal World".* (Third of six lectures on "Animals in Archæology". Further lectures on May 26, June 2 and 9.)

Wednesday, May 20

University of London (at the Institute of Diseases of the Chest, Brompton Hospital, London, S.W.3), at 5 p.m.—Dr. R. S. F. Schilling: "Recent Studies of Chronic Respiratory Disease in Cotton Workers".

Royal Statistical Society (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5.15 p.m.—Discussion on "Simulation Studies of Industrial Operation". Opening Speakers: Mr. P. V. Youle, Dr. K. D. Tocher, Mr. W. N. Jessop and Mr. F. Musk.

Eugenics Society (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Dr. Isabella Leitch and Mr. Angus Thomson: "Growth, Heredity and Nutrition".*

Society for Analytical Chemistry (at the Chemical Society, Burlington House, Piccadilly, London, W.1), at 7 p.m.—Meeting on "The Determination of Vitamin E; a Collaborative Study of Quantitative Paper Chromatography and the Development of a Recommended Method of Analysis".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Dr. M. F. Perutz, F.R.S.: "The Molecular Basis of Life".

Thursday, May 21

Institution of Mining and Metallurgy (at the Geological Society of London, Burlington House, Piccadilly, London, W.1), at 4 p.m.—Annual General Meeting. 5.15 p.m.—Dr. J. H. Watson: "Some Observations on Gold Refining and the Standard for Gold and Silver Coinage".

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. G. A. Maclachlan, Prof. Helen K. Porter, F.R.S.: "Replacement of Oxidation by Light as Energy Source for Glucose Metabolism in Tobacco Leaf"; Mr. S. H. Revell: "The Accurate Estimation of Chromatid Breakage and Its Relevance to a New Interpretation of Chromatid Aberrations Induced by Ionizing Radiations".

Physical Society (at the Royal Institution, Albemarle Street, London, W.1), at 5.45 p.m.—Mr. J. A. Ratcliffe, F.R.S.: Presidential Address.

Royal Society of Tropical Medicine and Hygiene (at Manson House, 26 Portland Place, London, W.1), at 7.30 p.m.—Dr. Ivan Polunin: "The Muruts of North Borneo and their Declining Population".

Thursday, May 21—Wednesday, May 27

International Transistor Exhibition (at Earls Court, London).*

Friday, May 22

Linnean Society of London (at East Malling Research Station, East Malling, Kent), at 11 a.m.—Meeting on "The Role of Plant Anatomy and Applied Botany".

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Lecturer (with high academic qualifications together with research or industrial experience in some branch of physics) in Physics—The Principal, Lanchester College of Technology, Butts, Coventry (May 21).

Assistant Lecturer in Geography, and a Junior Research Fellow in Geography—The Registrar, The University, Sheffield (May 23).

Head (graduate of a British university) of the Department of Mathematics—The Clerk to the Governing Body, Battersea College of Technology, London, S.W.11 (May 29).

Lecturer or Assistant Lecturer (qualified in applied mathematics) in Mathematics—The Registrar, University College of North Staffordshire, Keele, Staffs (May 29).

Dairy Officer (with a university degree in an agricultural science, preferably in dairying, or with postgraduate qualifications in dairying) in the Ministry of Agriculture, Federation of Rhodesia and Nyasaland—The Secretary (R), Rhodesia House, 429 Strand, London, W.C.2 (May 30).

Lecturer (Grade II), and an Assistant Lecturer (Grade III) in the Department of Zoology—The Registrar, The University, Bristol (May 30).

Research Assistant (graduate in chemistry or biochemistry), for work on urinary calculi in the Department of Veterinary Preventive Medicine at the Veterinary Field Station in Cheshire—The Registrar, The University, Liverpool (May 31).

Senior Lecturer or Lecturer in Physics at the University of Otago, Dunedin, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, May 31).

Assistant Editor (man or woman with a Ph.D. degree or equivalent research experience, and also some feeling for language, previous editorial experience not essential)—The General Secretary, The Chemical Society, Burlington House, Piccadilly, London, W.1 (June 1).

Lecturer in Mathematics, and an Assistant Lecturer in Mathematics—The Registrar, University College of Wales, Aberystwyth (June 5).

Assistant Lecturer in the Department of Zoology—The Registrar, University College of Wales, Aberystwyth (June 12).

Lecturer on Physiological Psychology—The Secretary of Faculties, University Registry, Oxford (June 15).

Lecturer in Pure Mathematics at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 20).

Senior Lecturer or Lecturer (with research or industrial experience with servo-mechanisms or in process control) in Control Engineering; a Lecturer (with a thorough knowledge of the physics of materials and preferably research or industrial experience involving solid state physics) in Materials; and a Lecturer (with good qualifications in light current electrical engineering or in physics) in Electronic Engineering—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (June 20).

Assistant Lecturer or Lecturer in Philosophy at the University College of Ghana—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (June 25).

Chair of Geography in the University College of Ghana—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (June 30).

Senior Lecturer in Mathematics at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, June 30).

Research Fellow (with M.Sc. or equivalent, with special knowledge and/or experience of agronomy of tropical crops) in Tropical Crop Production at the University College of Ghana—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (July 1).

Senior Lecturer or Lecturer in Philosophy at Canberra University College, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 4).

Lecturer (with an honours degree or higher degree in chemical engineering or equivalent qualifications) in Chemical Engineering at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, August 31).

Botanist (Plant Pathologist) (with a good honours degree in botany or agricultural botany and at least two years postgraduate experience in plant pathology) in the Department of Agriculture, Uganda, to diagnose the causes of crop diseases and recommend control measures, and to assist with the breeding of disease resistant crops—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/9/02.

Instructor or Assistant Professor in Protozoology—Dr. James R. Adams, Department of Zoology, University of British Columbia, Vancouver 8, Canada.

Lecturer and a Research Assistant (Academic) in the Physics Department, to take part in research in vacuum physics and photoelectronics applied to astronomy, nuclear physics, etc.—Prof. J. D. McGee, Physics Department, Royal College of Science, Imperial Institute Road, London, S.W.7.

Research Biologists (2) (with a science degree with honours in zoology), for research in introduced wild mammals in New Zealand, mainly species of deer—The New Zealand Forest Service, Wellington, New Zealand.

Research Engineers (2) (with at least an honours degree in mechanical engineering, or in some other specialization covering fluid mechanics, and preferably with some postgraduate experience) in the Department of Aircraft Propulsion, for theoretical and experimental work on the fluid mechanics of gas flow in solid rocket motors—The Recorder, The College of Aeronautics, Cranfield, Bletchley, Bucks.

Senior Lecturer in Biology—The Registrar, College of S. Mark and S. John, Chelsea, London, S.W.10.

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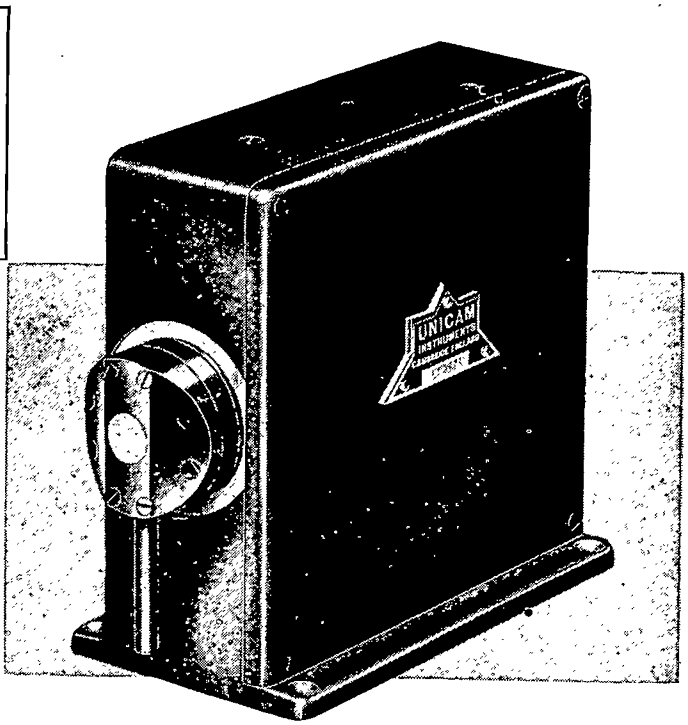

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BRITISH BOOKS AND INFORMATION SERVICES OVERSEAS

WHEN speaking in the debate on defence in the House of Commons on February 25, Mr. A. Head, a former Minister of Defence, said that his visits to South-East Asia, the Middle East and Africa in the past two years had increasingly convinced him that Britain is losing the battle for men's minds. It is, of course, as a contribution to this ideological warfare that President Eisenhower on March 13 asked Congress for 3,930 million dollars to continue the U.S. foreign aid programme, which includes 179 million dollars for technical assistance programmes in 1960 and 30 million dollars as a contribution to the technical co-operation and special projects programmes of the United Nations. An appreciable proportion of Colonial Development and Welfare Funds may be regarded as directed to the same end, and the stress laid on education at the Commonwealth Trade and Economic Conference at Montreal, and on information services, particularly on broadcasting and television, in the last annual report on the Colonial Territories, further indicates the growing realization of the importance of seeing that an accurate and objective picture of Britain is presented to the world.

It is against this background that the proposals outlined in the White Paper on Overseas Information Services* are to be considered. The plans outlined in the earlier White Paper of July 1957 led to an increase in expenditure on overseas information services, from £13 million to £15 million a year, chiefly through an increase in the number and strength of information posts, the re-deployment of external resources of the British Broadcasting Corporation, increased resources for the Central Office of Information, more television films, and a substantial expansion of the work of the British Council. Despite this expansion, details of which are appended to the new White Paper, annual reports of the British Council continue to testify to the inadequacy of the present effort, and in the last annual report Sir Charles Snow refers in particular to the unsatisfactory position of British books and other printed matter in the world overseas, including the Colonial territories. This has been the subject of persistent Parliamentary questions, and the travels of Dr. Charles Hill, Chancellor of the Duchy of Lancaster, to whom the survey of British information services was entrusted, have apparently shown him that British books are facing heavy competition in various areas, and convinced him that action is required. Nevertheless, in reply to Lord Stonehaven's request in the House of Lords on February 18 for a statement of the Government's plans for facilitating the increased distribution and sale overseas of British books and periodicals, particularly in countries where there are sterling restrictions, the Earl of Home could only state that Dr. Hill's study of these problems is well advanced and that a statement will be made as soon as possible.

On this question of books, the White Paper admits that there are countries where import restrictions hamper the British publisher in selling books at normal prices, although in these and other countries there are large numbers of students and others who cannot afford to pay anything like the ordinary economic prices for British books which they need or wish to read, and that other countries have done more than we have to devise ways and means of overcoming such obstacles. But it merely comments that the Government is studying ways of encouraging the flow of British publications overseas. Apart from this, the supply of books in existing British Council libraries is to be increased and more resources made available for the presentation of books to universities and other libraries. In addition, financial provision is being made for a pilot scheme of lending books to university and technical students in some countries for the duration of a course or session without the requirement to return the borrowed books in a fortnight or month. At present, Sir Charles Snow puts the total cost of British expenditure on the dissemination of the printed word at less than £500,000.

In replying in an adjournment debate on March 26 on the supply of British books and films overseas, Dr. C. Hill amplified the information given in the White Paper. There are ninety-nine British Council libraries, and help is given in maintaining about forty others. In the current year, £60,000 was spent on new books for these libraries; next year this will be increased to £171,000, and expenditure on periodicals will also increase. As regards exports of books, in 1937 the total value of books sold was £10·5 million and 30 per cent were exported; for 1946 these figures were £27 million and 24 per cent; and for 1957, £60 million and 37 per cent; in terms of individual books, probably about half the production is exported. Dr. Hill pointed out that the two British book export schemes have been closed down for political reasons in the countries concerned; he gave no further indication of the Government's intentions, though he re-affirmed that the study of the problem is almost complete. He pointed out that it need not be Government money which is blocked, and that Government action is not the only way of dealing with the problem. He regards the teaching of English and the provision of books, directly or through libraries, as the most important part of our long-term information work, and hopes for a general discussion before long on British Overseas Information Services as a whole.

The Government announced in the House of Commons on November 3, 1958, that a more intensive effort is required to ensure that British ideas, policies and objectives are widely known and understood, and the proposals outlined in the white Paper will increase the expenditure on overseas information services by a further £1·5 million. The expansion is designed particularly to meet changing conditions and techniques in parts of Asia and Africa, particularly the demands arising out of the desire for education; although it should be pointed out that the White Paper gives scant attention to the possibilities of television, beyond observing that there is considerable scope for the establishment or development of television services in some Commonwealth and Colonial countries, and that much preliminary work is proceeding. Dr. Hill was questioned on this point in the House of Commons on March 16 and agreed as to the great and increasing demand which we are seeking to satisfy. The English language is in wide and growing use throughout the world as the language of education, administration, culture and technology, and it is this fact that gives such importance to the teaching of English, including the supply and placing of teachers, and the supply of the books and periodicals needed to sustain and increase its use. This is apart from the need to demonstrate continuously the merits of a free as compared with a totalitarian society, to show the British understanding of the aspirations of other nations and to counter hostile misrepresentations of our aims and achievements.

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* Overseas Information Services. Pp. 8. (Cmnd. 685.) (London: H.M. Stationery Office, 1959.) 6*d*. net.

To do all this effectively requires, too, the maintenance of the reputation of British information services for accuracy and objectivity; but it should not be necessary to elaborate further the nature of these tasks to demonstrate how large a contribution this £16·5 million could make to the easing of the tasks of diplomacy and defence. As regards the British Council, the Government's proposals, which will increase the Council's grant to about £5 million, include the provision of more money to subsidize teaching posts, encourage exchanges of university teachers, offer more scholarships in Britain and provide special British Council officers to advise on problems in teaching English. The Council's work in Nigeria is to be strengthened, and provision made for exchange of visits and other activities in the educational and cultural fields with Czechoslovakia and Hungary.

On broadcasting, the growing listening public which local sound broadcasting stations command almost everywhere, and the increasing difficulty which short-wave transmissions from afar encounter in competing with medium-wave and very high-frequency programmes locally transmitted is emphasized, and the growing demand for recorded material on disk or tape for inclusion in local programmes is noted. To strengthen the signal of the Arabic, Somali and Swahili services, a new relay transmitter is to be completed at Berbera in the Somali Protectorate by the beginning of 1960, and the daily hours of transmission of the Arabic service of the B.B.C. are to be increased from 9·5 to 12 with increased coverage of events of local significance and greater local appeal in entertainment programmes. More help is to be offered to local broadcasting stations, particularly in eastern Africa and Aden, to which substantial grants have already been made from Colonial Development and Welfare Funds.

New posts are to be opened in the official information services and existing posts strengthened in New Zealand, South Africa and East Africa; but the main expansion of these official services will be in the production of material in the vernacular languages, as well as in English, for all Commonwealth countries, and in the improvement of communications. Special attention is being given to news items about people from overseas who are working or studying in the United Kingdom. More trade and technical periodicals will be distributed overseas, and the programme of visitors from overseas is again being expanded, especially for those from the Commonwealth.

The extent to which all this affects directly the work of the scientist and technologist is not very apparent from the White Paper itself, although it is obvious that measures to improve interchange, the flow of information—of the printed word and over the air—and to facilitate understanding and communication both within and without the Commonwealth must assist that increased scientific and technical co-operation for which the Duke of Edinburgh recently pleaded at Karachi. Moreover, the official services can never replace the work of the voluntary organizations, such as scientific societies. Some indication of the extent of present developments can, however, be gathered from the last annual report of the British Council, which during 1957–58 assisted more than 1,800 visits of scientific specialists to and from Britain—some 35 per cent of the total assisted. Indeed, of visitors to the United Kingdom in 1957–58 under the auspices of the British Council, 18·5 per cent were concerned with social studies, 42·6 per cent with science, 10·1 per cent with medicine, and 14·8 per cent with education, and the shift in subject pattern from the arts and humanities towards the pure and applied sciences is growing. British scientific books and periodicals form a considerable proportion of the Council's libraries, especially in those countries where interest in the sciences is high. While the scientist and technologist therefore will welcome the increased support to be given to overseas information services as indicated in the White Paper, the further statement of policy regarding measures to assist the flow of British books will be awaited with no less interest and even some anxiety. Until some measures have been taken to deal with the obstacles to the flow of British books abroad our economic and commercial interests, no less than those of science and technology, will continue to suffer, and British technology will not be effectively exported. Even such achievements as the nuclear reactor cannot be properly exploited if the relevant scientific and technical literature is not freely available. The full effect of at least some of the measures promised in this White Paper awaits action on the decisions to which it is to be hoped Dr. Hill's study will speedily lead him. Beyond this, however, the scientist or technologist who goes abroad should himself be among the best of Britain's interpreters, and possibly professional organizations and bodies responsible for young scientists and technologists going abroad for the first time could do more than at present to see that such recruits understand what is expected of them, the conditions they will meet and the equipment of mind and character as well as technique that they should take with them.

DEVELOPMENTS IN ADULT EDUCATION

Trends in English Adult Education

Edited by Prof. S. G. Raybould. Pp. xiii+258. (London: William Heinemann, Ltd., 1959.) 21*s.* net.

THE most remarkable feature of this book is that it should have been written at all. During the great debate of less than ten years ago some of the contributors to the book vociferously championed the pure white flag of liberal adult education and completely rejected all the mixtures which went under the false colours of extension classes, local education authority activities, informal pursuits, broadcasting and the like. Yet here is a book, more than half of which is concerned with trends quite unrelated to the traditional conception of adult education in Great Britain. It is a fine tribute both to the vigour of adult education itself and to the flexibility and resource of those who promote it.

With two exceptions, the contributors are all drawn from the department of adult education at the University of Leeds. They, and particularly the editor, deserve warm praise for setting down their recent experiences in such forthright, objective and yet provocative fashion; this applies no less to the two distinguished contributors from outside the University walls.

The great debate about the purpose and content of adult education was sparked off by Prof. S. G. Raybould himself in 1949. The issue, quite simply, was whether or not the time-hallowed name of adult education could be given to any activities unconnected with the tutorial classes which had been jointly developed by the Workers' Educational Association and university extra-mural departments. How the debate proceeded—and how other adult education activities developed apparently with the connivance of those who opposed them—is carefully set out in a well-written chapter by Roy Shaw. This, surely, should have been the starting point of the book.

The controversial place of the Workers' Educational Association in the adult education movement of to-day is carefully analysed by a great friend of the movement, J. F. C. Harrison. Regretfully he arrives at the only possible conclusion that the Association is but a shadow of its former self, has failed to adjust its aims and organization to the needs of 1959, and with bewilderment and frustration arising from lack of national leadership, stands in marked contrast to the buoyancy and optimism which marks the university adult education movement of to-day.

The latter is described by J. W. Saunders. Since 1945 the virtual monopoly of university services by the Workers' Educational Association has been challenged by education directly provided by the extra-mural departments of the universities, now recognized as 'responsible bodies' by the Ministry of Education. Besides traditional classes for the 'workers', extra-mural departments are providing an ever-increasing number of specially designed courses to appeal to specialized professional people and to students who have had the privilege of a secondary and even a university education; "new social purposes, new social fulfilments are being met". If, as Sir Charles Morris writes in the foreword to this book, "at all stages a great part of education must always be self-education", the university extension movement is surely right to give urgent attention to the quality and standard of people who emerge from schools and universities into a world of specialists.

Other chapters describe the increasing attention paid to adult education by local authorities; the direct contribution of broadcasting and, incidentally, the value of market research in giving the customer what he requires; the immeasurable value of residential adult education colleges by their most worthy exponent, Guy Hunter; the educational influences of organizations such as Women's Institutes, Townswomen's Guilds and various local societies; some experimental work in trade union education which needs to be followed up with much greater enthusiasm than appears to be the case; and finally, a review by Prof. Raybould of developments since the Ashby Report was published in 1954. Most of the recommendations set out in that Report have been implemented; their influence on adult education trends have been considerable. One recommendation made by the committee was that sooner or later adult education must fight for a due share of the finances of universities, instead of continuing to be a branch of university activity protected by ear-marked grants from the Ministry of Education. Prof. Raybould believes that the time to adopt this recommendation has arrived. His views are earnest and compelling and could well initiate another great debate.

T. H. HAWKINS

THE PSYCHOPATHOLOGY OF SCIENCE

The Sleepwalkers

A History of Man's Changing Vision of the Universe. By Arthur Koestler. Pp. 624. (London: Hutchinson and Co. (Publishers), Ltd., 1959.) 25*s.* net.

THE story of the substitution for the tight, cosy, Earth-centred world of Aristotle of the infinite, centreless, mechanistic universe of Newton is a drama which the dullest of historians could not conceal; it is told again by Mr. Koestler with all the stylistic verve of an experienced novelist and with adroit use of the materials and ideas pieced together by historians of science during the past two generations. Through detailed studies of Copernicus, Kepler and Galileo as examples of the medieval, the transitional and the 'terrifyingly modern' scientific mentality the author has succeeded brilliantly in giving the general reader a vivid account of what the change from medieval to modern cosmology involved. For this is the core of the book; nothing between Aristarchos and Copernicus holds much interest for Mr. Koestler, and his account of cosmology after Galileo is equally brief. Newton's austere mind commands his admiration, but not his imaginative sympathy.

Although he makes effective—not invariably quite accurate—use of recent work in the history of science, Mr. Koestler's opinions will not always commend themselves either to scholars or to scientists. He constantly under-rates Ptolemy's great achievement because he finds the theory of epicycles ridiculous, while recognizing that the epicycles were tools of mathematical analysis and not regarded as physical realities. Conversely, he argues that Galileo should have been satisfied with the status of the Copernican system as a "working hypothesis", since he could not prove its *de facto* truth. Yet the Church was only prepared to admit Copernicanism as a calculating device, precisely like Ptolemy's epicycles. To overlook this fact and to under-estimate Galileo's concern with physical reality rather than with mathematical hypotheses of planetary motion is to run in peril of the "double-think" that Mr. Koestler detects in others, and contributes to that lack of feeling for Galileo which is so marked and astonishing a feature of this book.

For Mr. Koestler is a violent partisan in the way he treats ideas and characters. For him Copernicus is a fumbler, a second-rate second-hand Aristarchos, cold, timid, anxious ; Galileo is arrogant, vain and deceitful, contemptuous of the achievements of others and rashly confident that he can over-reach the theologians, so precipitating a disastrous and unnecessary conflict. Kepler is the hero of the story because his scientific discoveries were the fruit of his mystical leanings ; Galileo its villain because he turned his back on Kepler and constituted himself the champion of science against religion. All this forms an interesting and provocative point of view ; but it is a highly personal one.

Not less singular is Mr. Koestler's chief term of historical appreciation : schizophrenia. The tension he finds in the history of cosmology he attributes to "split-mindedness" and its product "double-think". This journalistic distortion of a precise psychopathological concept may itself be deplorable to purists : it becomes objectionable to historians when the whole of the Middle Ages is dismissed as an age of the split mind, and to physicists when quantum mechanics enters the category of "double-think" (whatever that may mean). Perhaps one should not insist on an author's idiosyncrasy ; in this book, however, psychological theorizing is fundamental to the interpretation of history, and to the conclusions of the epilogue on the contemporary state of scientific thought. In short, the brilliance of the book lies in the literary use of recent historiography ; Mr. Koestler's allusions to the mental hospital give it an additional and perhaps more dubious colour.

A. R. HALL

THE PINNIPEDIA

Seals, Sea Lions and Walruses

A Review of the Pinnipedia. By Victor B. Scheffer. Pp. x+179+32 plates. (Stanford, Calif. : Stanford University Press ; London : Oxford University Press, 1958.) 30*s*. net.

THE Pinnipedia are a highly specialized group of about thirty species, which present unusual difficulties to the systematist. Their large, greasy skins are difficult to preserve, and are consequently scarce in museum collections ; the skeletal parts, especially skulls—on which the systematist has usually to rely for comparative material—in some cases undergo progressive change of form and proportion as the animal's age advances. Particularly in the various polygamous species the males do not stop growing at maturity, as do most warm-blooded vertebrates, but may continue to increase in size, in some species quite rapidly, throughout life. Consequently the average measurements of a sample can be materially affected by the age-composition of the group from which it was taken. In these circumstances the diagnosis of subspecies often proves almost impossible, and the boundaries between species and genera sometimes appear indefinite also. In the past, confusions of names have been common and synonyms are therefore unusually numerous.

No comprehensive synopsis of the Pinnipedia has appeared since the early years of the century, and this makes Dr. Scheffer's modern, practical and authoritative review of their taxonomy and distribution particularly welcome. I notice with interest that he feels the group ought to be regarded as an order in its own right, separate from the Carnivora. Fifteen of the twenty genera into which he divides the present-day forms are monotypic ; among these is *Phoca*, to which only the common or harbour seal (*P. vitulina*) is here assigned. Seals are characteristically distributed coastwise, often strung out in long chains rather than occupying broad regions, and this may have facilitated speciation. In none of the five polytypic genera is there any instance of two species in the same genus (as defined by Scheffer) occurring together in the same area.

Some of the more widespread species have disrupted ranges : the harbour seal, for example, has two distinct North Atlantic centres, one on each side, and two corresponding ones in the Pacific. Here the author has decided to assign separate subspecific names, notwithstanding the fact that constant physical differences between the races are not always discernible. The name *mellonae* is applied to a fifth, freshwater population in Ungava, "not because it stands for a remarkably different kind of seal but because it represents a situation . . . ". Such an unorthodox criterion is presumably justified by the convenience of having labels for populations which are geographically distinct and definable as living entities.

The systematic section is prefaced by fifty pages of highly condensed, almost laconic information, chiefly on the anatomy, physiology and evolution of seals. The introduction contains an illuminating table in which the world populations of all the numerous forms are critically estimated ; one recent race—the fur-seal of Juan Fernandez—is probably extinct, and some others are dangerously low ; but considering the ravages that seals and their allies have suffered all over the world at the hands of man they have shown surprising powers of resistance and recovery.

The book contains distribution maps, excellent photographs and figures, and a very full bibliography. Only systematic names are listed in the index ; but some indication of the numerous topics included in the book can be gleaned from the subheadings to the introductory chapters, given in the table of contents. It is a very useful work of reference.

V. C. WYNNE-EDWARDS

BRITISH WATER BEETLES OF THE FAMILY HYDROPHILIDAE

British Water Beetles

Vol. 3. By Prof. Frank Balfour-Browne. Pp. liii+210. (London : The Ray Society, 1958. Sold by Bernard Quaritch, Ltd., 11 Grafton Street, W.1.) 30*s*.

PROF. F. BALFOUR-BROWNE is much to be congratulated on having produced a third volume on British water beetles. The first two volumes, published in 1940 and in 1950, deal with the Hydradephaga, the present volume with the aquatic

Hydrophilidae. The author writes with intimate knowledge of the species dealt with, acquired during his long experience as a field naturalist. As in the previous volumes, no descriptions are given of the species, and a successful identification is dependent on the correct interpretation of the keys, aided, however, by many useful figures illustrating anatomical features. An account of the life-history of the Hydrophilidae is included in the introduction, and many interesting biological notes are scattered throughout the book. More information on the larvæ and their habitats—where these are known—would have been of much value, but it is hoped that this book will induce others to study the biology of these interesting beetles, as Prof. Balfour-Browne has done so ably in the case of *Hydrobius fuscipes*, L.

The maps showing county and vice-county boundaries are a great improvement on those given in the earlier volumes, and are most useful in showing at a glance the known distribution of a species. Few errors have been noticed in the text, but no map is given of *Ochthebius minimus* Fab. though quoted on p. 160, and many authors are mentioned without inclusion in the bibliography. An interesting account is given of the male genitalia in some species of *Ochthebius*, *Hydrœna* and *Hydrochus*. The author considers that the modifications described render the males of some species incapable of mating and he believes that in consequence parthenogenesis occurs. This is a problem requiring investigation.

Highly controversial are the author's views given under the heading "Distribution and Means of Transport", though what transport he envisages for flightless water beetles is not specified. His outlook on the problem of the present distribution of water beetles is dominated by his idea of recent "invasions" arriving not only at the coast from the Continent but accounting also for the occurrence of various local species, adapted to special habitats, in all parts of the country, such as *Helophorus tuberculatus* Gyll, in Lanark (p. 96). The occurrence of uncommon species in localities not previously or recently worked is no proof of their recent arrival, and especially is this true when the specimens collected are incapable of flight, as in the case cited (p. lii) of *Noterus crassicornis* Müll., a species which is common in a Fife loch where 90 specimens have been taken, all brachypterous. It is more likely that local aquatic species are the last remnants of a population that was formerly much more extensive, before drainage and cultivation had destroyed many habitats.

Argument is an excellent stimulus to further research, and Prof. Balfour-Browne has written a stimulating book which will arouse fresh interest in these beetles and prove of much value to the specialist.

Dorothy J. Jackson

THE ELUSIVE PARTICLE

The Neutrino

By Prof. James S. Allen. (Investigations in Physics, No. 5.) Pp. viii+168. (Princeton, N.J.: Princeton University Press; London: Oxford University Press, 1958.) 36s. net.

This small book gives an excellent description of experimental work on the neutrino, which only in the past few years has been shown to have any direct physical property apart from balancing energy, momentum and spin in β-decays. It is a tribute to modern methods of experiment that neutrino-capture in hydrogen has been demonstrated by Reines and Cowan in spite of the fact that a neutrino beam could traverse a thickness of solid material measured in *light years* without appreciable loss. The timing of the book was unlucky, because it was written before or during the revolution which occurred in the last half of 1957 and in 1958, due to the discovery of the non-conservation of parity in β-decay. Dr. Allen was therefore obliged to cover the changes in "Notes added in Proof". This he has done satisfactorily, but the subject has been so much changed very recently that a much clearer picture would be possible now.

Nevertheless the book is a useful one since it is concerned mainly with descriptions of experimental methods in the very difficult field of neutrino physics, and does not go into details of theories, some of which have changed.

The subject has had a curious history. Experimentalists were misled for many years by the conservation of parity theory, which was not based on any universally valid evidence, into not looking for such an easily detectable phenomenon as the polarization of electrons in β-decay. Some wrong results in the electron-neutrino angular correlation experiments, understandable in view of their difficulty, also contributed to the confusion. However, now everything seems in order on the two-component neutrino theory of Lee and Yang, both for β-decay and for pion decay. It has not happened often that so tricky a field of physics has been cleared up so quickly, as a result of brilliant theoretical work, which suggested many key experiments.

H. W. B. Skinner

LEGENDRE FUNCTIONS

Fonctions Sphériques de Legendre et Fonctions Sphéroidales

Tome 2. Par Dr. Louis Robin. (Collection Technique et Scientifique du C.N.E.T.) Pp. viii+384. (Paris: Gauthier-Villars, 1958.) 5,300 francs.

The second volume of Dr. Robin's comprehensive treatise deals with the associated Legendre functions $P^m{}_n(\mu)$, $Q^m{}_n(\mu)$. The problem of defining these functions for unrestricted complex values of m, n and μ was tackled by several mathematicians in the late nineteenth century, and finally solved by Hobson (1896), who used for this purpose the double-circuit contour integrals devised by Jordan and Pochhammer. An essentially complete theory was expounded in full in Hobson's classical treatise on spherical harmonics (1931), and Dr. Robin has based his book very largely on this work, with some extensions and some elaboration of detail. There are three sections. In the first, which occupies more than half the book, the formal discussion of the functions is developed in exhaustive fashion. In the second, asymptotic formulæ and the Stieltjes-Hobson inequalities are considered; in the third, convergence and summability of series of Legendre functions. The influence of Hobson and of other British mathematicians, for example, Barnes, Watson, MacRobert, is very evident, and little of importance has escaped the author's attention. The book is for reference rather than for light reading, and for British readers is scarcely likely to replace Hobson; but Dr. Robin has taken account of work done since 1931, and has also incorporated earlier work, for example, on

Cesàro summability (C, k) with $k<\frac{1}{2}$, which is only briefly referred to by Hobson.

In 1908, Barnes gave an alternative to Hobson's definition, using a contour of integration parallel to the imaginary axis and a gamma-function integrand. Dr. Robin refers to this and also to Barnes's penetrating study of asymptotic expansions. But since Barnes's work has never been published in full, and since he claimed that his methods diminish the labour to about one-third of that required on Hobson's approach, it would be interesting to see what, for example, the first section of Dr. Robin's book would look like if written out on Barnes's lines. This, however, would in no way detract from the value of the present volume as an admirable work of reference.

T. A. A. Broadbent

AVIAN FOLKLORE

The Folklore of Birds

An Enquiry into the Origin and Distribution of some Magico-Religious Traditions. By Edward A. Armstrong. (The New Naturalist: a Survey of British Natural History.) Pp. xvi+272+33 plates. (London: William Collins, Sons and Co., Ltd., 1958.) 30s. net.

Birds have always fascinated humanity. Only of recent years has proper attention been paid to the importance of folklore for the study of history and of the way people thought in the past. It is only just in time. Folktales and folklore were seldom written down but were passed from generation to generation by word of mouth. Nowadays the spread of so-called civilization has meant that, except here and there in outlying districts, everything has been forgotten. Recently there has been a move to collect what has survived and to examine at the same time the folk legends of modern primitive peoples. Fortunately, although not written down, pictures recalling the folklore have often been used as decorative motifs in peasant crafts, and a close study of these has helped to elucidate the underlying legends. Of course, not every figure of a bird either in prehistoric times or at a later period illustrates some myth or legend. Indeed, I doubt whether the bird-sign on the top of a staff which can be seen in the Under Cave at Lascaux in connexion with the happy looking rhinoceros walking away from the disembowelled bison nearby is anything but the sign manual of some hunter concerned with the painting of the scene. This may well have been made for some definite purpose, though not necessarily to illustrate what we should to-day call folklore. Whether one can talk about folklore as such in palæolithic times one may be allowed to doubt, but in the later periods there is often documentary evidence which explains some of the art.

Edward A. Armstrong is well known as a naturalist. He has written much on bird life, and his book, "The Wren", is deservedly popular. In the present volume he starts with early times and continues with chapters devoted to various species of birds which figure especially in folklore tales. Thus we find chapters on the goose, the red-throated diver, the raven, the green woodpecker, the eagle, the wren, and a number of song birds. Each chapter describes some of the legends attached to the particular bird or group of birds. There is also an account of the beliefs which have grown up in various places, that the dead return as birds; for example, the story of the fisherman seeking his dead brother who had foretold that he would return as a gannet after death and would be recognizable by his black armsleeves. The author has thrown out his net widely. In time he ranges from prehistoric to recent periods, and geographically from Hudson's Bay to Zimbabwe in Rhodesia. There are numerous and delightful illustrations, some line blocks, some in half-tone and one in colour. The book as a whole is a scholarly account of the subject and a great deal of material has been collected. It also makes good reading. Archæologically and anthropologically it is a work which the purchaser will find well worth possessing.

M. C. Burkitt

RESEARCH ON HORMONES

Recent Progress in Hormone Research, Vol. 14

Proceedings of the Laurentian Hormone Conference 1957. Edited by Gregory Pincus. Pp. vi+582. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1958.) 13.50 dollars.

The fourteen articles contained in this volume record the contributions and discussions at the 1957 meeting of the Laurentian Hormone Conference. Hormones are chemically diversified and include among their number proteins, polypeptides, steroids, and catechol amines. Their biological effects embrace practically all vital processes, while their applications to medicine include both psychiatry and general medicine. It is therefore inevitable that the good endocrinologist must keep in touch with many different sorts of research, and books like this one assist him to remain in contact with aspects of the subject which otherwise might be difficult to follow.

The first section of the book, devoted to a series of four papers on "Hormone Structure and Function," well illustrates how often small changes in chemical structure can profoundly alter biological activity. The actions considered in this section range from the inhibition or facilitation of the growth of tumours to the regulation of electrolyte metabolism. The next section, dealing with "Hormones in Growth and Development," contains three papers and is largely directed towards hormonal influences on protein and fat synthesis and catabolism. It includes a discussion of the effects of hormones in cattle production, and in mammary development and function. The third section is concerned with "Reproduction", and from this section can be seen how developmental abnormalities can profoundly influence the secretion of hormones and how in their turn the activity of hormones can play a part in sex development. The section on "Hormones and Metabolism" includes a discussion on the effect of hormones on lipoprotein and connective tissue metabolism. Finally, a section on "Neurohumors" includes a discussion of adrenaline, noradrenaline and their striking influence on many different processes.

The book includes discussions on subjects which embrace specialized organic chemistry, tumour growth, cattle raising, sex pathology, atherosclerosis, anxiety neuroses, and senescence. Hormones link the tesserae of this fascinating mosaic and it is perhaps not to be wondered at that the variety of subject and diversity of activity in the field of endocrinology continue to challenge many active minds.

F. G. Young

MICROSCOPY WITH X-RAYS*

By Dr. V. E. COSSLETT
Cavendish Laboratory, University of Cambridge

THE idea of making a microscope for X-rays goes back to the earliest days of the subject. In the original announcement of his discovery, Röntgen[1] describes an attempt to focus the new radiation and concludes from its lack of success: "das man mit Linsen die X-strahlen nicht konzentrieren kann, ist nach dem Mitgeteilten selbstverständlich". Although later experiments have shown that, in fact, a focusing effect exists, it is so small that an X-ray microscope on the lines of the usual optical microscope would be impracticably long. However, the advantages of using X-rays are so considerable that many attempts have been made to devise systems which do not include lenses. X-rays penetrate matter relatively easily, they offer the possibility of a higher definition of image than with light, and, more important, they are emitted (and absorbed) in a manner specific to the nature and amount of the elements present, so that analysis on the microscale becomes possible.

Reflexion Focusing

If X-rays are incident perpendicularly on a mirror, they pass straight into it and the amount reflected is negligible; but if the beam just grazes the surface, reflexion is almost 100 per cent efficient. Since all materials have a refractive index slightly less than unity for X-rays, total reflexion occurs for a beam passing from air into any physically denser material such as glass or metal. Hence it is possible to focus X-rays with a curved mirror, so long as they fall on it at glancing incidence. The 'critical angle' is very close to 90°, and so the glancing angle has to be less than 1°, at the wave-lengths so far employed. In consequence, scarcely any focusing takes place at right angles to the plane of incidence, so that the image formed by a concave mirror of spherical curvature is drawn out into a line: the focusing is highly astigmatic. As pointed out by Kirkpatrick and Baez[2], however, a second mirror in a plane at right angles to that of the first will produce a stigmatic image. Focusing systems of this type have been developed by Kirkpatrick and his school at Stanford University[3]. The alignment of the mirrors and the position of the object are somewhat critical at such small angles of incidence, and micrometer adjustments are required. Single-stage microscopes only have so far been built, since a compound microscope would involve undue loss of intensity in the succession of reflexions as well as great difficulty in alignment. The best results, obtained with test grids, approach the performance of a good optical microscope. McGee[4] claims a resolving power of about 0·5 micron, using mirrors of radius 8·5 metres and focal length 6·4 cm. To keep the exposure time within reasonable bounds (10–30 min.), he worked with a direct magnification of seven times only.

The obstacles to further development of the reflexion system are of two types: aberrations of the image, and practical difficulties in making the mirror surfaces. Lack of image brightness, giving long exposures, is also a limitation, since the aperture cannot exceed the grazing angle of total reflexion, that is, about 1°. The aberrations of the focusing system can in principle be overcome by using combinations of several mirrors with surfaces of special form — elliptical, paraboloidal, hyperboloidal — as shown by Wolter[5] and Pattee[6]. The correction obtainable with a pair of crossed ellipsoids followed by a pair of crossed paraboloids should give a resolving power of 500 A.—about twice as good as the ultra-violet microscope and four times better than the limit of the optical microscope.

The preparation of such corrected systems demands great skill and patience in polishing the surface to the required degree of perfection—about ten times better than that called for in the best optical practice. Not only must the surface be true to the particular aspherical form computed, it should also be smooth to almost molecular dimensions. For these reasons, it is difficult to estimate the ultimate performance to be expected from the reflexion X-ray microscope. It seems probable that the same definition as in the best optical microscope will be reached, but less likely that the limit predicted by Pattee is within practical possibility.

Contact Microradiography

The simplest way of obtaining enlarged images is by geometrical projection, dispensing with any form of focusing system, as in the usual method of medical radiography. Specimens partially transparent to the radiation, as most will be, form half-tone images rather than simple silhouettes. The limiting factor to the definition obtainable is set by the penumbra, formed at the edge of the true shadow. The definition can be increased, if microscopical detail is sought, either by reducing the size of the source or by moving the specimen close to the viewing screen (or photographic plate). The former, or projection method, allows high direct magnification, by bringing the specimen close to the source. The latter method yields no initial magnification, all the enlargement being obtained by subsequent viewing of the negative through an optical microscope; it has come to be known as 'contact microradiography'. So long as the X-ray source is far enough away for the penumbra to be of negligible width, the definition in the final image is determined by the size of grain in the developed emulsion and by the resolving power of the optical microscope used to enlarge it. With modern fine-grained emulsions, as prepared for spectrographic purposes, these two factors are of about equal order, namely, about 0·2–0·5 micron, so that the best contact microradiographs have almost as good a definition as the best optical micrographs.

The technique was developed, largely in France, between the two World Wars. Since 1946 it has been brought to a high art by Engström and his co-workers in Stockholm, especially for cytological studies. The first recorded application was to the study of the internal structure of alloys, however. Heycock and

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* Substance of a Friday Evening Discourse delivered at the Royal Institution on February 6.

Neville[7], at the laboratory of Sidney Sussex College, Cambridge, in 1898 investigated the differences in size and shape of the precipitates formed when an aluminium–gold alloy was cooled quickly and slowly. Since that time the method has been gradually introduced into metallurgical practice, as in the work of Sharpe[8] and Andrews and Johnson[9] in Great Britain, and Trillat[10] in France. The applications in biology have been much more widespread, and have been recently reviewed by Engström[11]. By using very soft X-rays, it is possible to show clearly even cell components so small as a chromosome, without staining or otherwise interfering with them.

The great advantage of the contact method lies in its simplicity, and in the large field of view recorded. No special X-ray tube is required, though the exposure time can be cut appreciably (to 20 min. or so) by using one properly designed for the purpose[12,13]. The fine-grained emulsions demand careful handling, in dust-free conditions, on account of the high subsequent magnification that is needed. For highest definition, the specimen must be prepared as a thin section and brought into close contact with the emulsion, and Engström has developed special techniques for this purpose. In definition the ultimate limit is set by the resolving power of the optical microscope, so that a resolving power better than about 0·2 micron is not to be expected. The best contact micrographs from Engström's laboratory already approach this limit.

Projection Microradiography

In the projection method the specimen is placed close to the source, instead of close to the photographic plate, and a point source becomes the essential requirement in place of an ultra-fine grained emulsion. A point source is most simply obtained by placing a small aperture before an X-ray source of normal size, and the first 'pinhole-camera' radiographs were made in this way by Czermak in 1896[14]. The intensity of the beam through such an aperture was very small, however, and even with the improved tubes that later became available, it was impossible to combine appreciable magnification with reasonable exposure time (Sievert[15]). In 1939 it was pointed out by von Ardenne[16] that a point X-ray source of great brilliance could be formed by using magnetic lenses to focus the electron beam on to the target of an X-ray tube, the definition in the projection image being then limited primarily by the size of the source.

A point-projection system of this type was later constructed by Cosslett and Nixon[17] at the Cavendish Laboratory. To obtain a high demagnification of the electron source (a tungsten filament), two electron lenses are employed. The electron spot at the target can then be made smaller than 1 micron without difficulty, and even as small as 0·1 micron. The X-rays issue from this focal spot through the very thin target, which serves as window to the tube. An object placed close to it will form an enlarged image on a screen or plate at a distance. Since the source–object distance may be as small as 0·1 mm., a direct X-ray magnification of 100 × is obtainable in a camera-length of 1 cm., or of 1,000 × in 10 cm. The voltage on the tube has usually been in the range 5–20 kV., and the electron beam current is of the order of 1 μamp., concentrated into a focal spot of 1 micron or less. The dissipation of heat from such a small electron spot is so favourable that no water cooling of the target is needed.

The range of applications of the projection method is somewhat wider than that of the contact method, which is restricted by the need to have the specimen close to the recording emulsion. For example, it is better suited to the study of living subjects. Saunders[18] has followed up the earlier contact work of Barclay[19] and Bellman[20] in the field of microarteriography, and has studied the circulation in the ear of the rabbit under the influence of various treatments. The thickness of specimen that can be tolerated is greater than in the contact method, and may be as much as 1 mm. Smith[21], for example, has investigated the musculature of a series of beetles in the projection X-ray microscope. The whole of the internal structure is visible at once, whereas by optical techniques it would have to be worked out from a set of consecutive sections through the insect, owing to the limited depth of focus of the light microscope. A large number of other applications in mineralogy and metallurgy, in entomology and in botany, have also been explored.

In the projection system the depth of focus, in effect, extends all the way from the near side of the object to the photographic plate. It is thus possible to make stereophotographs of specimens much thicker than could be tolerated in the optical microscope; in the latter the focal depth decreases as the useful magnification increases, so that stereophotography at high power is impracticable. Excellent X-ray stereomicrographs have been obtained of alloy structures and of insects. Although it is possible to make stereophotographs by the contact method, it is more trouble both to make the initial pictures and to identify the same area in the two negatives.

The projection method is to be preferred for microradiography whenever the area of interest can be readily identified, by optical or other means, and mounted in the X-ray beam for the production of a direct image. On the other hand, the contact method provides a much larger initial field of view, from which areas can later be selected by exploration of the micronegative under the optical microscope. The exposure-time of the projection method is shorter by a large factor, being of the order of 1 min. The resolving power is limited, not by that of the optical microscope, but by the size of the electron spot on the target and the extent to which electrons are scattered in it before producing X-rays. The best results so far obtained by Nixon[22] and by Ong and Le Poole[23] are in the region of 0·1 micron, the limit of resolution of the ultra-violet microscope. The projection method thus already gives a higher resolving power than either the reflexion or contact methods. Further progress is at present hindered by lack of intensity, since the current that can be focused into the focal spot falls rapidly as its diameter is made smaller, but there is good reason for supposing that the resolving power will be improved to 0·05 micron (500 A.) and fair hope that it will reach 250 A.

Microanalysis by Differential Absorption

Both the contact and the projection methods of microradiography may be used to determine the nature and proportion of the chemical elements in a specimen, by making use of the steps which occur in the absorption spectra. The absorption coefficient of a given element changes abruptly at a well-defined wave-length, whereas that of the matrix in general increases smoothly and approximately in proportion to the cube of the wave-length. The steps are relatively infrequent, so that it is rare for the wave-lengths for two elements to be too close to be separable with an X-ray spectrometer. If measurements of X-ray transmission are made at wave-lengths just below and just above that of a step, then the difference will be due to the presence of the corresponding element, after allowing for the small change in absorption by the matrix. Knowing the height of the absorption step for the pure element, the observed height gives at once the percentage of it present in the matrix. By this means practically all elements in the Periodic Table may be determined quantitatively.

In the contact technique it is necessary to take micrographs of the specimen at two selected wave-lengths for each of the elements to be estimated. The difference in absorption in particular regions is found by measuring the relative transparency of the negative with a microphotometer. For accurate work, the photographic processing has to be carefully standardized, and it is preferable to make measurements on the original negatives rather than on enlargements. The smallest area that can be analysed is then limited to that of the smallest light spot which can be formed in the microphotometer—about 5 sq. microns. Lindström[24] has carried out micro-analyses of sulphur, phosphorus and calcium in sections of certain biological tissues, with an ultimate sensitivity of between 10^{-11} and 10^{-12} gm. and a relative accuracy of ± 3 per cent. On the other hand, if only the amount of matter present per unit area is of interest, as in many cytological investigations, an absorption measurement at a single wave-length is sufficient, provided that the composition of the absorber is known within certain limits. By this means Engström[11] has been able to make determinations of the dry weight of cell constituents with an accuracy almost as good as that achieved by the interference microscope.

Absorption microanalysis is more easily carried out by the projection method, since it is then unnecessary to make a photographic negative: the relative transmission of different points in the specimen is measured directly by placing an aperture, behind which is a spectrometer and counter, at the required points in the projected image. Röckert[25], in conjunction with Long[26], measured the micro-distribution of calcium in the cementum layer of the teeth of monkeys of different ages, and taken from different positions in the jaw. It turned out that there was no significant trend: the variation for a tooth of given type, in different individuals, was much greater than the variation in the average value with age or position. Long has used the same technique for determining calcium in a number of minerals, and Mosley and Wyckoff[27] have made qualitative surveys of other elements.

Emission Microanalysis

An alternative method of elementary analysis is by spectrometry of the characteristic emission lines excited when the specimen is made the target in an X-ray tube. From the position of the lines the elements present may be identified and intensity measurements give their relative concentration. By comparison with pure standard samples, the absolute amount of each element can be calculated.

The method has been practised on large-scale specimens for a long time, both by direct excitation on the target of a tube and by fluorescent excitation, in an intense primary X-ray beam. Its application on the micro-scale was first made by Castaing and Guinier[28]. They employed electron lenses to form a point focus of electrons on the specimen, placed inside the tube, and analysed the X-rays excited at a particular point in its surface, selected by means of an optical microscope built into the electron lens. Improvements now allow all elements in the Periodic Table, from uranium down to aluminium, to be analysed to an accuracy of 0·1 per cent in areas of diameter about 1 micron. Such a static spot X-ray microanalyser is now in production in France.

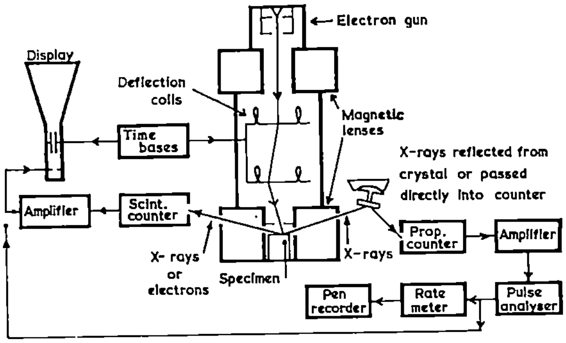

Fig. 1. Schematic diagram of X-ray scanning microanalyser

It would be helpful to be able to see exactly what point in the surface of the specimen was being struck by the electron spot. The flying-spot technique, already applied in optical and electron microscopy, was therefore combined with the microanalyser[29], as shown schematically in Fig. 1. The X-ray output is detected with a counter, amplified and used to modulate the beam of a cathode-ray tube operating in synchronism with the scan of the electron beam across the target. If the undifferentiated output is so displayed, an image is obtained of the specimen surface in terms of its total emissivity of X-rays. If a particular emission line is selected, the image shows the distribution of the corresponding element over the specimen, the local brightness depending on the amount of the element present at that particular point. By 'tuning-in' to each element present, a semi-quantitative analysis of the area scanned can be quickly carried out. When the elements are not near neighbours in the Periodic Table, the necessary selection of the emission lines can be made with a proportional counter alone, but with next neighbours it is at present essential to use a Bragg spectrometer. The collected intensity is then lower and a slow scan has to be used, the image being formed on a screen of appreciable 'memory' (long-delay tube), in order to gain a storage effect.

If a more accurate analysis is required, the electron spot can be made to scan along a given line and the output fed to a pen recorder, which traces out the variation in amount of the selected element across that part of the surface. Alternatively, the scan may be stopped and the electron spot moved by manual control to a point of special interest. The relative intensities of the X-ray lines of the various elements present are then recorded on a chart as the spectrometer selects them from the emitted spectrum (Fig. 2). After correction for differential absorption in the target and recording system, an accuracy of 0·05 per cent can be obtained in favourable cases, but the accuracy falls with the amount of element

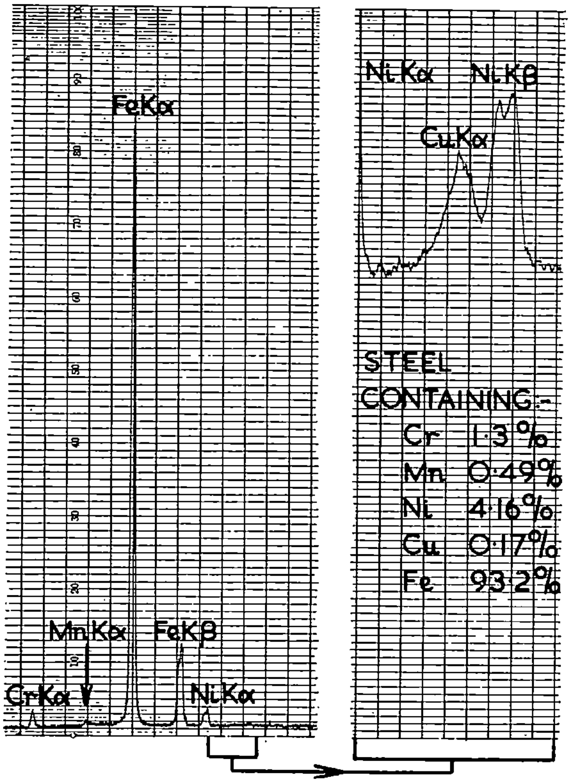

Fig. 2. Analysis of steel with the X-ray microanalyser

present. The electron spot can be made as small as 1 micron in diameter without undue loss in signal strength, so long as a high proportion of an element is present. At the voltages used on the tube (15–25 kV.), the electron beam penetrates a few microns into most metals before its energy falls too low for excitation of their characteristic X-ray lines. A volume of a cubic micron or so can thus be analysed, containing a mass of about 10^{-11} gm., and the sensitivity, the smallest amount that can be detected, is between 10^{-14} and 10^{-15} gm. Although some methods of analysis can give greater accuracy of determination, and one or two methods can equal the sensitivity, none can provide anything like the same degree of microscopic localization as in the X-ray microanalyser. For this reason it is finding increasing application in metallurgical[30], mineralogical[26,31,32] and, to a lesser extent, biological research.

The original scanning microanalyser was made by adapting an old electron microscope. An improved model has now been constructed at the Tube Investments Research Laboratories, Hinxton, which will be used for metallurgical investigations. It allows three spectrometers to be trained on the specimen, so that three elements can be analysed simultaneously. The scanning system has now also been incorporated in the Castaing-type microanalyser constructed at the A.E.I. Research Laboratory, Aldermaston, and shown at this year's Physical Society Exhibition. A simpler instrument has recently been built by Long[26], designed primarily for mineralogical work. Since most rock sections are thin enough to be optically transparent, a microscope is built into the side of the vacuum chamber, so that the section may be searched to select areas of interest for scanning; a fluorescent glow usually appears where the electron spot strikes it. As before, an image is displayed on a long-persistence cathode-ray tube screen, showing the surface distribution of a particular element in the rock, or the variation in concentration along a line may be shown. By using a double-beam display tube, the concentration can be graphed immediately above the trace of the path along which the analysis is made. For high accuracy, a pen recorder may be coupled up in place of the double-beam oscilloscope; but where an analysis to no better than 1 per cent suffices, it may be obtained directly from the photograph of the latter. A number of microanalyses of minerals and meteorites has been made[26,31,32].

The further development of the emission microanalyser faces the difficulty that the X-ray intensity decreases as the size of spot is reduced. Duncumb has analysed precipitates as small as 0·25 micron, with a spot rather larger, but the signal was very weak. Analyses of still smaller regions can certainly be made with the instrument as it is; but the time required becomes prohibitive for routine operation, and the output is insufficient for visual observation. Intensity might be increased in three ways: by improved design of the electron gun; by correction of the spherical aberration of the electron lenses; and by collecting a greater proportion of the emitted X-rays. Research on all three lines is in progress in the Cavendish Laboratory and elsewhere. There is reasonable prospect of substantial improvements, especially in the third direction, and we may expect to be able to analyse particles as small as 0·1 micron in the near future.

The other main problem is the extension of the range of elements that can be analysed, from aluminium down to nitrogen and carbon. The detection and separate estimation of these elements is of great importance for ferrous metallurgy, where carbides and nitrides abound. If this can be done—and the prospects are encouraging[33,34]—then the scope of the X-ray microanalyser will be greatly increased, and it might also become of value to the biologist. At the moment, it is possible to detect and estimate the concentration only of heavier elements that may be present in pathological conditions, such as tin or silica in the lung. Even when carbon, nitrogen and oxygen can be analysed, however, it remains doubtful if it could be done without charring the tissue or otherwise removing constituents selectively by the electron bombardment. The usefulness of emission microanalysis for the biologist must therefore remain an open question until more experience has been gained. In metallurgy and mineralogy its value is already established, and it is now a question of exploring its limits. The peculiar combination of microscopic imaging with microanalysis appears to be more powerful, within its range of resolution, than any other optical or electron optical methods yet devised, so that the new technique, whether or not one admits its classification as a microscope, is rapidly finding a place of its own among research tools.

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HETEROGENEITY IN DEOXYRIBONUCLEIC ACIDS

I. Dependence on Composition of the Configurational Stability of Deoxyribonucleic Acids

By Dr. JULIUS MARMUR and Prof. PAUL DOTY

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THE base-pair interactions that unite the two chains of deoxyribonucleic acid in its native, helical configuration are of two kinds: adenine–thymine and guanine–cytosine[1]. Because these pairs involve different numbers of hydrogen bonds[2] and are otherwise dissimilar, it is to be expected that they contribute differently to the stability of the helix. We wish to report here the magnitude of this effect (which is substantial), its use in estimating the extent of heterogeneity in composition within samples of deoxyribonucleic acid and to some degree within its molecules, and its importance in inactivation studies.

Upon heating neutral solutions of deoxyribonucleic acid, striking changes in some properties[3] (for example, viscosity, extinction coefficient, light scattering and optical rotation) are known to occur in a relatively narrow range of temperature. These changes reflect a transition from the double-stranded helical configuration to a disordered coil: the transition is essentially the melting of one-dimensional crystallites and may be characterized by the temperature at the midpoint of the transition, T_m. In earlier studies[4] on calf thymus deoxyribonucleic acid there appeared some indications that the transition consisted of a series of overlapping transitions of individual deoxyribonucleic acid molecules having different melting temperatures.

In particular, the transition was broader than expected for such very long, perfectly formed helices, and at temperatures within the transition region the viscosity would quickly reach a constant value and fall further only if the temperature was increased[5]. Furthermore, electron microscopy revealed that within the transition region only two types of deoxyribonucleic acid molecules could be discerned, namely, completely denatured or native ones[6]. The most reasonable explanation lay in assuming that the two hydrogen-

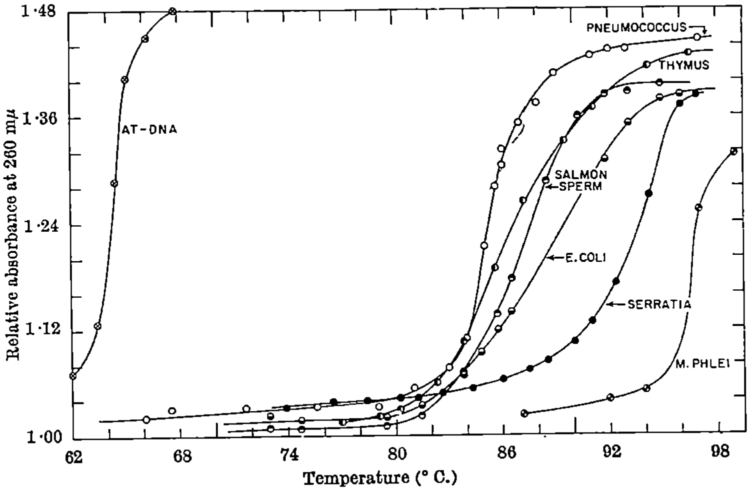

Fig. 1. Variation in absorbance (260 mμ) as a function of the temperature of the deoxyribonucleic acid solution. The result for bacteriophage T_4r deoxyribonucleic acid is not plotted because of serious overlap with *D. pneumoniae*. It was sharper and had T_m equal to 84°. In all cases the solvent was 0·15 *M* sodium chloride plus 0·015 *M* sodium citrate. The samples of bacterial deoxyribonucleic acid were deproteinized by successive mild shakings with chloroform and *iso*amyl alcohol. The samples of animal deoxyribonucleic acid were prepared by the Simmons technique using detergents (see ref. 5). The bacteriophage T_4r deoxyribonucleic acid was a gift from Mr. J. Fleichman

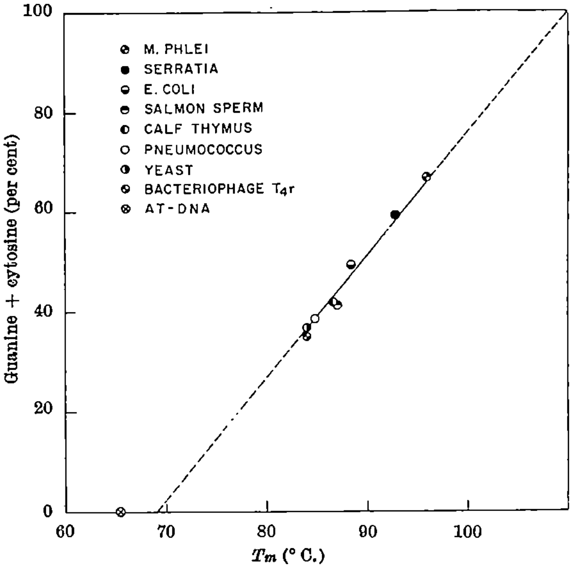

Fig. 2. Dependence of the denaturation temperature, T_m, on the guanine–cytosine content of various samples of deoxyribonucleic acid

bonded base pairs (guanine–cytosine and adenine–thymine) contributed unequally to the stability of the helix, thereby causing T_m to depend on the mean composition of either whole deoxyribonucleic acid molecules or large segments thereof.

In order to test this proposal, we have prepared a number of protein-free samples of deoxyribonucleic acid of different base composition from various sources (see Fig. 1) and determined their transition profiles by measuring the absorbance at 260 mμ as a function of the temperature of the solution. These are recorded in Fig. 1, and the melting temperatures are plotted as a function of the guanine–cytosine content[7] in Fig. 2. In the solvent used (0·15 *M* sodium chloride and 0·015 *M* sodium citrate), it is seen that T_m ranges from 85° C. for deoxyribonucleic acid from *Diplococcus pneumoniae* to 97° C. for that from *Mycobacterium phlei* in a manner directly proportional to the guanine–cytosine content. The T_m values are reproducible to within 0·5 deg. for different carefully prepared samples, and hence they may be considered as intrinsic characteristics of total deoxyribonucleic acid from a given species.

The extrapolation of the results in Fig. 2 permits an estimation of the T_m of deoxyribonucleic acid made exclusively of one base-pair or the other; for adenine–thymine this is 69° C. and for guanine–cytosine it is 110° C. The gift of a sample of adenine–thymine deoxyribonucleic acid[8] allowed us to check one of these predictions. The melting profile is shown at the extreme left of Fig. 1; its T_m value is 65° C. (In contrast to samples of naturally occurring deoxyribonucleic acid, the absorbance–temperature curves of which are far from being reversible, this adenine–thymine deoxyribonucleic acid exhibited complete reversibility. This behaviour would only be possible if the adenine–thymine sequence was strictly periodic.) In addition to verifying the dependence of T_m on composition, the magnitude of the hyperchromicity observed for this sample (52 per cent) supported the trend seen in the naturally occurring deoxyribonucleic acid samples between the hyperchromicity and the composition. In these the hyperchromicity decreased from about 44 to 34 per cent as the guanine–cytosine content increased from 38 to 67 per cent. Thus, in the limit of pure guanine–cytosine deoxyribonucleic acid, the hyperchromicity would probably be only about 25 per cent. Of course, this can only be a rough correlation, because the hyperchromicity in a given sample probably depends on sequence as well as overall composition.

An estimate of the dispersion of the guanine–cytosine content among the molecules of a given sample can be made in the following way. The melting profile of the adenine–thymine deoxyribonucleic acid, since it is of high molecular weight ($S_{20,w}$ = 12·6 *S*.) and with no heterogeneity due to composition, can be assumed to represent the natural transition width due to the intrinsic nature of this co-operative phenomenon. The displacements of this curve from its T_m can then be subtracted from the other melting profiles to give corrected profiles that should reflect only the spread due to heterogeneity of composition. This has been done for the samples studied with the following results. The transition of T_4r bacteriophage deoxyribonucleic acid had the same sharpness as the adenine–thymine deoxyribonucleic acid; hence the deoxyribonucleic acid molecules in this case appear to have essentially identical composition. The profiles for *D. pneumoniae* and *M. phlei* were only slightly broader. The remaining samples of bacterial deoxyribonucleic acid showed increased broadening of the transition, indicating significant heterogeneity in composition. The broadest profile is that from calf thymus; the central part of this transition (50 per cent of the rise in absorbance) covers about 4°. Since the slope of the line in Fig. 2 equates a change of 1 deg. in T_m to a 2·5 per cent change in composition, the half-width of the distribution of guanine–cytosine residues in calf thymus deoxyribonucleic acid can be estimated as extending ± 5 per cent about the mean of 49 per cent guanine–cytosine.

With calf thymus deoxyribonucleic acid appearing to have a relatively broad distribution of composition, an attempt was made to recover undenatured deoxyribonucleic acid from a partially denatured sample and to see if it had a higher melting profile. A sample heated to 90°, corresponding to 80 per cent of the transition, was cooled and carried through two successive precipitations with streptomycin. The resulting sample exhibited a melting curve that was displaced 1·5 deg. higher than the calf thymus curve in Fig. 1. Thus, it is seen that components of different T_m are indeed contained within calf thymus deoxyribonucleic acid.

In a further experiment, calf thymus deoxyribonucleic acid was degraded sonically to one-twelfth of its original molecular weight. Its melting profile was then only very slightly broadened. This indicated that the heterogeneity observed here exists on a scale very much smaller than that of whole molecules.

The relatively small dispersion in the distribution of guanine–cytosine among the samples of bacterial deoxyribonucleic acid, viewed in conjunction with the very broad range of mean composition, leads to the interesting conclusion that there is essentially no overlap in the composition of the deoxyribonucleic acid molecules of many bacteria. This point is confirmed and discussed in the following communication.

The relation between the transition profile and the inactivation of the transforming ability of *D. pneumoniae* deoxyribonucleic acid has been examined in two ways. When this deoxyribonucleic acid undergoes extensive inactivation by ultra-violet irradiation, no significant changes in its macromolecular properties can be detected. However, the transition profile is relatively sensitive to irradiation, being shifted to successively lower temperatures. For example, at 10 per cent remaining streptomycin transforming activity, T_m is 1·5 deg. lower. Thus, what is generally considered to be a very small amount of chemical alteration can be detected by the alteration of the absorbance–temperature profile.

When the thermal inactivation of various genetic markers is compared with the transition profile, it is found that the inactivation generally lags behind to varying degrees. This may arise either from a partial reversibility of the transition, that is, a re-healing of some molecules that are only partially melted out, or from our happening to select markers that are carried by the deoxyribonucleic acid molecules having higher T_m values.

We wish to thank Miss D. Lane, Mr. J. Kucera and Mr. L. Matthews for essential contributions to experimental work presented here. We are grateful to Drs. J. Fresco and N. Sueoka for helpful discussions. This investigation has been supported by a grant from the U.S. Public Health Service, C-2170.

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II. Dependence of the Density of Deoxyribonucleic Acids on Guanine–Cytosine Content

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The discovery by Meselson, Stahl and Vinograd[1] of a technique of banding deoxyribonucleic acids in the density gradient established in the cell of an analytical ultracentrifuge has made possible the precise determination of the density of samples of deoxyribonucleic acid in microgram amounts. With this sensitive method available, it was of interest to see if a variation of density with guanine–cytosine content could be detected that would parallel that found for the denaturation temperature, reported in the foregoing communication. A systematic examination of samples of deoxyribonucleic acid having different guanine–cytosine contents showed that there was indeed a significant dependence. We wish to summarize these results here and to indicate the use of this effect in estimating the heterogeneity of composition in deoxyribonucleic acid samples and in studying the denaturation of deoxyribonucleic acid. The estimates of heterogeneity of composition for samples of bacterial deoxyribonucleic acid are unexpectedly small; the implications of this are briefly discussed.

The experimental technique employed was precisely that described by Meselson *et al.*[1]. About 3 μgm. of deoxyribonucleic acid was added to a concentrated solution of cæsium chloride (about 8 *M*) adjusted to the anticipated density. This was centrifuged in the 'Spinco' Model E ultracentrifuge at 44,770 r.p.m. at 25° C. for 24 hr. By this time the deoxyribonucleic acid had banded and its distribution in the band had become essentially constant. The distribution was recorded by photographing the cell using ultra-violet light and making a microdensitometer trace. As an illustration of the effect observed, Fig. 1 shows a photograph of a solution containing nearly equal amounts of four samples of deoxyribonucleic acid and the corresponding trace. The resolution of the four bands is evident. The results of a systematic study are shown in Fig. 2, where the density is plotted against guanine–cytosine content. It is seen that a linear relation is found; it corresponds to a change of 0·00103 in density per 1·0 per cent change in guanine–cytosine content. Since the uncertainty in determining densities in this way is about 0·001, it follows that the guanine–cytosine content of a sample of deoxyribonucleic acid can be determined from its density with a precision of about 1 per cent.

The extrapolation of the results for naturally occurring deoxyribonucleic acid to the extremes of the composition axis indicates that adenine–thymine deoxyribonucleic acid should have a density of 1·662 and guanine–cytosine deoxyribonucleic acid 1·764. The measured density for the former is 1·680. The difference may be attributed to the adoption of a slightly more compact structure when guanine–cytosine pairs need not be accommodated[2].

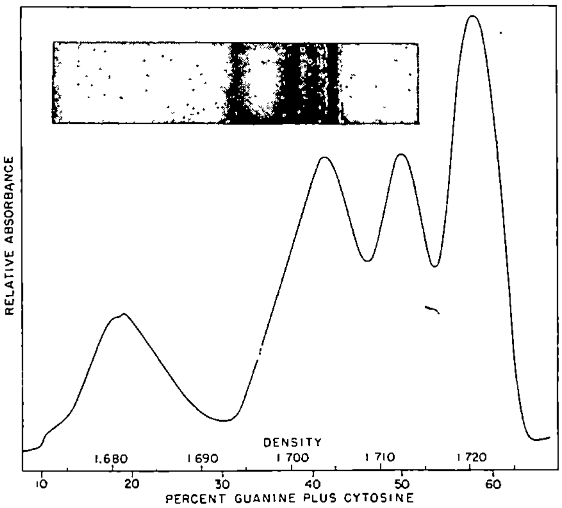

Fig. 1. Resolution of polydeoxy adenine–thymine and *Pneumococcus*, *E. coli* and *Serratia marcescens* deoxyribonucleic acids by density-gradient centrifugation. The photograph was taken after centrifugation at 44,770 r.p.m. for 24 hr. The tracing was taken with a microdensitometer in the region of the four bands. (The composition scale does not apply to the adenine–thymine deoxyribonucleic acid)

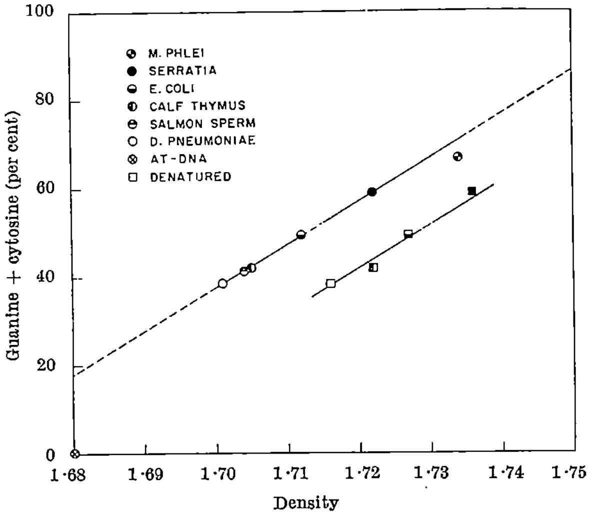

Fig. 2. Relationship of density to the guanine–cytosine content of various samples of deoxyribonucleic acid

At least half the observed dependence of density on composition can be explained by differences in the molar volumes of the two base-pairs as computed from atomic volumes. The failure to explain the entire difference in this way may lie either in errors inherent in deriving molar volumes from atomic volumes or from a small dependence of the atomic co-ordinates of the structure of the deoxyribonucleic acid on base-composition[2], or from an unequal binding of cæsium chloride ions by the two base-pairs.

Having found that the density of deoxyribonucleic acid depends on its composition, it follows that a heterogeneity of composition among the various deoxyribonucleic acid molecules of a given sample will be reflected in a broadening of the band. Molecules of uniform density are distributed in the band region as a result of thermal agitation. Meselson *et al.*[1] have shown that the square of the standard deviation, σ^2, that is, the variance, was inversely proportional to the molecular weight. However, if a distribution of density is superimposed upon the molecules, there will be a further broadening of the band. It will be useful to examine the relative importance of these two effects in a specific example.

Under the conditions employed, the relation between the molecular weight, M, and the variance is $M = 239{,}000/\sigma^2$, where σ is expressed in mm. Thus, in the absence of heterogeneity of density, deoxyribonucleic acid of molecular weight 8,000,000 would have $\sigma = 0{\cdot}172$ mm. The half-width of the band would be approximately double this distance, that is, 0·35 mm. Let us ask what heterogeneity of composition would have to be introduced to increase the band-width by $\sqrt{2}$, that is, to diminish the apparent molecular weight to 4,000,000. Since, under the conditions of these experiments, the density gradient $d\rho/dr$ was equal to 0·0122 mm.$^{-1}$, it follows that the formal dependence of composition on distance is $(d\rho/dr)/(d\rho/dX) = dX/dr = 0{\cdot}0122/0{\cdot}103 = 0{\cdot}1185$ mole fraction unit per mm. Since the σ due to heterogeneity of density must be equivalent to 0·172 mm., a standard deviation of 0·0204 mole fraction units is required in the distribution of composition to provide for an increase in the band width by $\sqrt{2}$. Thus, a distribution of guanine–cytosine such that the half-width of the distribution is 4 per cent on the guanine–cytosine scale would cause a sample of deoxyribonucleic acid having a molecular weight of 8,000,000 to appear to have a molecular weight of only 4,000,000. This degree of heterogeneity of composition lies in the range estimated from the analysis of the absorbance–temperature curves for bacterial deoxyribonucleic acid (see preceding communication). Consequently, the heterogeneity of composition encountered in samples of bacterial deoxyribonucleic acid can be large enough to affect appreciably the molecular weight calculated from band-profiles. Conversely, the band-widths observed for these samples of bacterial deoxyribonucleic acid are sufficiently small to set an upper limit to the heterogeneity in composition. Thus, even if the entire band-profile is interpreted in terms of density heterogeneity, we can conclude that this corresponds to a relatively narrow distribution of molecular composition about the mean composition. Our estimate of the heterogeneity in composition of calf thymus deoxyribonucleic acid is consistent with the fractionations that have been reported: however, only approximate comparisons can be made. The five fractions obtained by G. L. Brown and A. V. Brown[3] indicate a distribution having a little greater dispersion than that which we estimate. The three fractions obtained by Crampton, Lipshitz and Chargaff[4] as well as the selected fractions of Bendich *et al.*[5] show a somewhat smaller range (41–48 per cent guanine + cytosine). Our estimate for the heterogeneity of calf thymus deoxyribonucleic acid is that the σ-value is approximately equal to 0·06 mole fraction units; that is, the half-width of the curve of distribution against composition would extend from about 37 to 49 per cent guanine + cytosine. It is to this point that we shall return at the end.

In the absence of heterogeneity of density, the band-profile should be symmetrical. In samples of two mammalian deoxyribonucleic acids, calf thymus and mouse, pronounced skewness has been found. These are on opposite sides in the two cases. An unsymmetrical heterogeneity of density provides an obvious explanation for this effect.

With the means at hand for estimating the distribution of guanine–cytosine content among the molecules of a sample of deoxyribonucleic acid, it is of interest to see to what extent this heterogeneity is maintained within the deoxyribonucleic acid molecules. Since the distribution of composition is found to be relatively narrow, it would be expected that it would broaden as the molecules were degraded. Since sonic waves can be used to degrade deoxyribonucleic acid without denaturation[6], this problem may be approached as follows. We assume that the total variance of a band is equal to the sum of the variance due to thermal agitation and to the variance due to the distribution of density. If the molecular weight can be obtained for the original deoxyribonucleic acid and for one or more sonically degraded samples, the variance related to molecular weight can be computed. When this is subtracted from that found from the band-profile, the remainder should in each case be that due to the heterogeneity of density, and at sufficiently advanced degrees of degradation it should increase. In a preliminary experiment along these lines we degraded sonically calf thymus deoxyribonucleic acid from its original value of 8,000,000 to 620,000. The broadening of the band-profile was found to be actually somewhat less than that expected from the fall in molecular weight alone and, incidentally, the skewness remained.

Consequently, in this case we conclude that the distribution of composition found for the deoxyribonucleic acid molecules is preserved down to at least a tenth the original molecule.

When deoxyribonucleic acid is thermally denatured, the density increases. The results for four samples are plotted as square symbols in Fig. 2. The average increase of 0·015 compares very well with the earlier observation of an increase of 0·014 for two samples by Meselson and Stahl[7].

In an earlier study of thermal denaturation of calf thymus deoxyribonucleic acid[8], it appeared that the sample consisted of molecules having a range of individual denaturation temperatures, and this can now be interpreted as resulting from the distribution of guanine–cytosine. When partially denatured calf thymus deoxyribonucleic acid was examined in the density gradient, it was found that the band corresponding to the original deoxyribonucleic acid had diminished principally at the expense of material of low density, and that the new band which appeared had a lower density than completely denatured deoxyribonucleic acid. This behaviour clearly indicates that those molecules of relatively low guanine–cytosine content had become preferentially denatured. It has already been mentioned that the isolation of native deoxyribonucleic acid from such a partially denatured sample had a higher melting temperature (see preceding communication). When this fraction was examined in the density gradient, it was found to have a correspondingly higher density than the original deoxyribonucleic acid from which it had been isolated. Thus, the earlier views on the denaturation of deoxyribonucleic acid are confirmed and extended by recognizing explicitly the role of the guanine–cytosine heterogeneity.

In conclusion, we return to comment on the surprising finding that samples of bacterial deoxyribonucleic acid have a relatively narrow range of base composition, while the mean compositions show a wide variation. This stands in contrast to the nearly identical base compositions of mammalian deoxyribonucleic acid. The result for bacterial deoxyribonucleic acid is surprising, because it shows that bacteria having deoxyribonucleic acid density differences of 0·02 or more have essentially no deoxyribonucleic molecules with common composition. Since the metabolism and replication of bacteria do have much in common, it is generally thought that many of their proteins should be identical, or very similar. Yet all current discussions of the way in which deoxyribonucleic acid can control the sequence of amino-acids in protein requires a direct correlation between the composition of the deoxyribonucleic acid and of the protein.

Since it is often assumed that the information in deoxyribonucleic acid passes to the protein through ribonucleic acid, it is of interest to note that Belozersky and Spirin[9] have demonstrated that the variation in composition of bacterial ribonucleic acid is relatively small, but nevertheless it does show a significant correlation with the composition of the corresponding deoxyribonucleic acid for nineteen bacterial species.

It appears that the explanation of this dilemma with regard to bacterial deoxyribonucleic acid must lie with one of three possibilities.

(1) The proteins that perform common functions in bacteria may be structurally quite different in many cases. For example, in enzymes the active sites may be similar, but the main part of the proteins different. This is the situation that might be expected if the evolutionary development of bacteria has followed a number of independent paths, each corresponding to the elaboration of a complex genome from a primary deoxyribonucleic acid of a particular composition. In general, this view suggests that the distribution in composition of deoxyribonucleic acid molecules of organisms reflects their phylogenetic relationship.

(2) The proteins that perform common functions in bacteria are very similar structurally. If all the deoxyribonucleic molecules are genetically active and yet unrelated in composition in many cases, the coding between the deoxyribonucleic acid and the protein must be very different from those that have been considered hitherto[10]; that is, it has been customary to assume that the sequence of amino-acids (20) in proteins is coded in the sequence of the four nucleotides in deoxyribonucleic acid. Since it has been shown that various triplets of nucleotides are sufficient to specify each amino-acid, it follows that similar proteins must be derived from deoxyribonucleic acid molecules of similar composition, unless quite artificial, *ad hoc*, restrictions are imposed. If the coding concept is to remain, a radical revision is necessary in order to eliminate this dependence on composition. For example, the four-letter alphabet (adenine, cytosine, guanine, and thymine) could be abandoned in favour of a two-letter alphabet in which adenine and cytosine (6-amino-bearing nucleotides) would serve as one letter and guanine and thymine (6-keto-bearing nucleotides) would serve as the other. In this case no relation to composition would be expected. Of course, it would be possible to retain the four-letter alphabet if it were assumed that different codes applied to different bacteria, but this alternative is unattractive because it is most unlikely that different codes would yield the same number of amino-acids (20).

(3) The proteins that perform common functions in bacteria are very similar structurally, and the current ideas concerning the coding problem remain acceptable. This could only be true if the major part of the deoxyribonucleic acid was genetically inactive. The minor part of the deoxyribonucleic acid could then have a composition in common with the corresponding part of other bacterial deoxyribonucleic acid. It appears that this minor part would have to be less than 10 per cent of the whole to have escaped detection.

The proof, or even the disproof, of any one of these possibilities would be very enlightening.

We wish to thank Prof. M. Meselson and Mr. J. Kucera for help in the initial stages of this investigation. This work has been supported by grants from the U.S. Public Health Service, C-2170, and from the National Science Foundation.

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NEWS and VIEWS

Geology at Exeter: Dr. Scott Simpson

Dr. Scott Simpson, at present lecturer in the University of Bristol, has been appointed professor of geology in the University of Exeter in succession to Prof. A. Stuart, who has retired (see *Nature*, 181, 87 ; 1958). After receiving his early education at Highgate School, Scott Simpson proceeded to Clare College, Cambridge, and in 1937 took the second part of the Tripos in geology, selecting the alternative papers in palæontology. His postgraduate training was at Frankfurt-am-Main, where the late Prof. Rudolf Richter set him the task of unravelling the structurally complex area of Devonian rocks between Mayen and Daun in the east Eifel. That success attended his efforts is clearly shown by the fact that Richter, rather characteristically, arranged for Scott Simpson to be formally awarded his doctorate by the University of Frankfurt-am-Main two years after the start of hostilities between Britain and Germany.

Scott Simpson was assistant lecturer in the Department of geology and mineralogy at the University of Aberdeen for the first two years of the Second World War before he was seconded for the next four years to the Department of Natural Philosophy, where he instructed Royal Artillery and R.A.F. cadets in elementary physics and also worked at the Radon Centre. He transferred in 1949 from a lectureship in geology at the University of Aberdeen to a corresponding academic post at the University of Bristol. Here during the past decade he has acquired a reputation as a recognized authority in Britain on the stratigraphy and palæontology of the Devonian rocks. His own researches in Devon, and those of his students, have already resulted in important correlations being made with Devonian rocks of parts of Germany, and the methods he has applied have resolved the complicated geology of large areas of Devon and Cornwall. Of recent years he has carried out pioneer work in the study of structures in sedimentary rocks due to burrowing organisms, and their interpretation in terms of the interplay of organic and sedimentary processes. His reputation extends beyond the British Isles and his researches are recognized in Germany, Holland and France.

The Editors regret that, due to difficulties in the printing industry, some sections of this issue of "Nature" have had to be curtailed

Development and Research Appointments at the Mond Nickel Co., Ltd. : Dr. W. Steven

Dr. W. Steven, superintendent of the Development and Research Department Laboratory of the Mond Nickel Co., Ltd., in Birmingham, is to be transferred on June 1 to the Development and Research Division of the International Nickel Co., Inc., New York, as director of research. He has also been elected an assistant vice-president of that company. Dr. Steven graduated in the University of Glasgow in 1939 and obtained his Ph.D. degree in 1942. After five years with William Jessop and Sons, Ltd., Sheffield, he joined the Mond Nickel Co. in 1947 as a research metallurgist. In 1955 he was appointed superintendent of the laboratory.

Dr. G. L. J. Bailey

Dr. G. L. J. Bailey has been appointed superintendent of the Mond Nickel Development and Research Department Laboratory in Birmingham in succession to Dr. Steven. He took a B.Sc. (Hons.) degree at the Imperial College of Science and Technology, London, in 1937 and obtained his Ph.D. in 1939. After working at the Admiralty Engineering Laboratory, West Drayton, he joined the British Non-Ferrous Metals Research Association, where he became deputy research manager. Since 1955 he has been superintendent of the Platinum Metals Research Laboratory of the Mond Nickel Development and Research Department at Acton.

Dr. W. Betteridge

Dr. W. Betteridge has been appointed superintendent of the Platinum Metals Research Laboratory of the Mond Nickel Development and Research Department at Acton in succession to Dr. Bailey. Dr. Betteridge graduated in physics at the University of Birmingham in 1931, obtained his Ph.D. in 1933 and his D.Sc. in 1958. After serving with Joseph Lucas, Ltd., and the Bristol Aeroplane Company, he joined the Mond Nickel Co. in 1947, where he has been concerned primarily with the development of high-temperature materials, at first in the Birmingham Research Laboratory and more recently as development officer in London.

Submarine Defence Research

In reply to a question in the House of Commons on April 29, the Parliamentary and Financial Secretary to the Admiralty, Mr. C. Ian Orr-Ewing, said that the North Atlantic Treaty Organization research centre on defence against submarines, which was being set up by SACLANT at La Spezia, would be financed, at least for the initial period, entirely by the United States, and was intended to augment the scientific effort devoted by the several Nato countries to anti-submarine warfare research. The centre would be concerned primarily with basic problems, but would also undertake some operational research. The number of British scientists and Royal Naval officers to be employed there was not yet settled, but the naval adviser on the Scientific Advisory Council which would direct the work of this unit would be the Chief of the Royal Naval Scientific Service.

Department of Scientific and Industrial Research : Lending Library

A list showing holdings of the Lending Library Unit of the Department of Scientific and Industrial Research of irregular serials being received from the U.S.S.R. and Bulgaria has been issued (pp. ii+90.

London : D.S.I.R., Lending Library Unit, 1959), the titles being arranged mainly in alphabetical order, using the Cyrillic alphabet. There is also a short list of serials received from Latvia, Lithuania and Estonia, published in the Roman alphabet. Besides an index of transliterated abbreviations of titles, arranged alphabetically, there is an alphabetical subject-list based on a broad framework of the Universal Decimal Classification. The items listed can be obtained by approved borrowers from the Science Museum Library, using loan requisition forms issued by that Library, but these should be sent direct to the Unit at 20 Chester Terrace, London, N.W.1.

The Royal Institution Library

THE Library of the Royal Institution, which contains about 65,000 volumes, is divided into five sections, comprising the old library—started in 1799 and including many of the early works of the great philosophers as well as books published up to 1857 and the notebooks, letters and papers of Count Rumford, Humphry Davy, Michael Faraday, John Tyndall and others ; the modern library—containing books published after 1857, arranged by the Gliss classification ; the lending library, devoted mainly to general and popular science ; the periodicals, of which 400 are currently received ; and the storerooms. Notes on the library and its catalogues, with a list showing the holdings of periodicals and serial publications currently received, are given in a pamphlet recently issued (pp. 28. London : Royal Institution, 1958).

Florida State Museum

THE Florida State Museum serves as a joint University–State Museum and its major functions are to assemble and maintain collections of cultural and natural objects ; to encourage research on this material ; and to disseminate knowledge by publications and display. The annual report for 1957–58 (pp. 20. Gainesville, Fla. : Florida State Museum, The University, 1959) indicates that these functions have been fully maintained. During the period under review the staff has concentrated on the improvement of display, and many new ideas and techniques, especially those including the effect of artistry in presentation, have been incorporated. The investigation of archæological sites that might have been damaged by road construction has continued.

Tetrahedron Letters

As a supplement to the journal of organic chemistry, *Tetrahedron*, the Pergamon Press (London and New York) has begun to issue fortnightly or monthly *Tetrahedron Letters*, in which short communications of interest to organic chemists will be published within a week or month of acceptance (subscription, post paid (air mail charges extra) : £7 or 20 dollars per annum for libraries, government departments and industrial establishments ; no extra charge for private subscribers to *Tetrahedron* who write direct to the publisher certifying that the subscription is for their personal use). The first number (pp. 35) was published in March and contains six short communications of an international character. This publication should relieve some of the pressure on other scientific journals and its high standard seems likely to ensure it the success it deserves.

Education of Instrument Technologists and Control Engineers

THE subject of Mr. J. F. Coales's presidential address on May 6 to the Society of Instrument Technology was well chosen. Having shown the growing need for larger numbers of control engineers and instrument technologists and having proved that in most industries to-day there is some form of automatic control, he proceeded to outline the types of courses suitable for the men in charge. His views on the education of control engineers coincide with those expressed by several speakers at the conference on Degree and Diploma Courses in Applied Physics, arranged by the Society of Instrument Technology in November 1956, particularly in his insistence upon a broad-based fundamental approach for the graduate. Appendixes to his address contained valuable information which could not be easily assimilated into the body of the address, and many will be particularly interested in Appendix 2, concerned with detecting elements, and Appendix 3, outlining syllabuses for the ordinary National Certificate in Instrument Technology. Appendix 2 contains some twenty-one examples out of more than two hundred listed in a recent report on "Detecting Elements" published by the British Scientific Instrument Research Association.

Cyanamid International : Technical Papers

CERTAIN technical papers prepared by the research workers of Cyanamid for presentation before various learned societies in the United States or for publication in the proceedings of technical institutions in that country are to be made available in Britain. These papers cover a wide range of subjects but fall roughly into three classifications : pharmaceutical, agricultural and industrial, these being the main spheres of activity in which the Cyanamid group of companies is engaged. From time to time lists are prepared showing details of the technical papers available for distribution. Readers who would like to receive these lists as and when they are issued should write to : Cyanamid International Information Service, 16 Bolton Street, London, W.1.

The Age of the Earliest Remains of Man

CERTAIN skeletal finds from caves in the dolomite formation of the Transvaal not far from Pretoria have been known for some time. Whether these are indeed the earliest known remains of true man or whether they must be considered as still prehuman remains a matter of controversy. The late Dr. van Riet Lowe described in *Nature* (175, 16 ; 1955) a series of chipped stones which he considered to be artefacts, so that the beings in question were tool-using creatures. But grave doubts have been cast on Lowe's opinion and the objects in question may be natural products. Their association with the skeletal remains is more than uncertain, and they are probably later in age. Nevertheless, these skeletal finds are of capital importance, particularly to the physical anthropologist, and it is especially important that the cave deposits containing the remains of the Australopithecinæ should be accurately dated. A detailed investigation by C. K. Brain has recently been published (The Transvaal Ape-Man - bearing Cave Deposits. By C. K. Brain, with an appendix by R. F. Ewer. Transvaal Museum Memoir No. 11. Pp. viii+131. Pretoria : Transvaal Museum, 1958). The book can be recommended as a clear, succinct and factual account of the problems involved. The first part comprises an account of dolomite caves in general and of their infilling. This part will perhaps be of greater interest to the geologist, but the prehistorian is unwise if he puts these matters completely on one side. Part 2 gives a detailed account of most of the known sites—Sterkfontein, Swartkraus, Kromdraai, Coopers *B*, and the Makapan limeworks. In a final chapter a correlation of the deposits in the various sites is given and their ages suggested. Using the Leakey fourfold system of pluviations, it would seem that these early beings must be assigned to a period between the Kageran and the Kamasian pluvials, that is to say, to the first inter-pluvial, except for Kromdraai, which is slightly younger and dates to the second pluvial period. If they are certainly human and an association with true artefacts can be proved, they are indeed the earliest remains of our species so far discovered. The appendix by R. F. Ewer lists the faunal remains found.

Bibliography on the Chemistry of Tobacco Smoke

"The Constituents of Tobacco Smoke: an Annotated Bibliography", edited by H. R. Bentley and E. G. N. Berry, is the third in a series of research papers published by the Tobacco Manufacturers' Standing Committee (pp. ii+49. London, 1959). This publication, with its attractive format, contains more than 600 references on tobacco smoke, drawn from the technical literature of the world on that subject. The earliest reference quoted is to a German work of the year 1826. There are eight sections, dealing with nicotine, bases, acids, phenols, hydrocarbons, neutral fraction, arsenic, and a miscellaneous section which includes such diverse components as trace minerals, carbon monoxide and free radicals. Each section is preceded by a short introductory comment. While nearly 200 substances are quoted as occurring in tobacco smoke, the editors wisely point out that the degree of precision with which identifications have been made is by no means uniform, so that some of the work reported is of questionable reliability. This publication should prove very valuable to workers in the field of tobacco carcinogenesis, where an active search for carcinogenic factors of human significance is under way, proceeding from the proposed causal hypothesis relating tobacco usage and human cancer. The minute quantities of traditional carcinogens of the aromatic hydrocarbon class found in cigarette smoke are unlikely to explain the proposed special carcinogenic environment of the cigarette smoker.

Books required for the "Oxford English Dictionary"

The Editor of the Supplement to the "Oxford English Dictionary" writes: "It has proved impossible to obtain copies of some works, now out of print, which would help in the preparation of the forthcoming Supplement to the 'Oxford English Dictionary'. Any readers who would be willing to give, sell or lend copies of any of the following are requested to get in touch with the Editor at: 40 Walton Crescent, Oxford.

"J. R. Carpenter, 'Ecological Glossary', 1938.
R. T. Glazebrook, 'Dictionary of Applied Physics', 1922–23.
Oliver Heaviside, 'Electrical Papers', 1892.
Henderson and Henderson, 'Dictionary of Scientific Terms' (we have edit. 6, 1957; earlier editions required).
B. D. Jackson, 'Glossary of Botanic Terms' (any edition).
'Radio Engineering Handbook' (edits. 1 and 2), 1933–35.
A. L. M. Sowerby, 'Dictionary of Photography' (we have the 18th edit., 1957 impression; earlier editions needed)."

Announcements

The Wenner-Gren Foundation for Anthropological Research has awarded Viking Fund Medals and Awards of 1,000 dollars to Prof. Raymond W. Firth (University of London); Prof. Henri V. Vallois (director of the Musée de l'Homme, Paris); and Dr. Jesse D. Jennings (University of Utah).

It was announced at a recent meeting of the British Section of the Louis Rapkine Association that the Cross of Chevalier de la Légion d'Honneur has been awarded by the French Government to Dr. G. E. W. Wolstenholme, director of the Ciba Foundation, in recognition of the work he is doing for international co-operation in medicine and science and more particularly for Anglo-French collaboration.

The Geological Society of London has awarded the Daniel Pidgeon Fund for 1959 in moieties to Dr. M. K. Howarth, who proposes to study the Alum Shales (Upper Lias) at Whitby with particular reference to the ammonite fauna, and to Dr. M. J. S. Rudwick, who proposes to undertake research into the functional significance of the morphology of fossil brachiopods.

Two open days will be held by the British Cast Iron Research Association during May 28 and 29. A number of special exhibits and demonstrations have been arranged. The first day is set aside for representatives of member-firms and for the Press, the second for representatives of Government departments, other research organizations, educational bodies, trade unions, users of iron castings, and others. Further information can be obtained from the Intelligence Department, B.C.I.R.A., Bordesley Hall, Alvechurch, Birmingham.

The fifth International Salon de la Chimie is to be held in Paris during June 18–29 in conjunction with the fifth Rubber and Plastics Exhibition, the eleventh Exhibition of Laboratory Equipment and Instruments, the fifth Exhibition of Chemical Engineering and Protection against Corrosion, the fifth Industrial Heating Exhibition, and the first Literature and Press Exhibition. Further details can be obtained from the General Secretariat of the Fifth Salon de la Chimie, 28 rue St. Dominique, Paris 7^e^.

The twelfth annual conference on Electrical Techniques in Medicine and Biology will take place in the Sheraton Hotel, Philadelphia, Pennsylvania, during November 10–12. It is sponsored by the Joint Executive Committee in Medicine and Biology, appointed by and representing the pertinent interests of the American Institute of Electrical Engineers, the Institute of Radio Engineers for its group on Medical Electronics and the Instrument Society of America. Proposals for papers are invited and should be submitted to Dr. L. E. Flory, RCA Laboratories, Princeton, N.J., before July 1. Such proposals should be 100–200 words in length, supplemented by a short biographical note, and include affiliation and company title.

Erratum. J. R. Hensler, Bausch and Lomb Optical Co., Rochester 2, New York, writes: "In my note, 'Synthesis of Colour Centres in Silica and their Thermoluminescence', published in *Nature*, March 7, p. 673, column 1, lines 3–6 should read: 'The quenching of the luminescence in the presence of the aluminium centres is evidence for the interaction of these and the ultra-violet absorbing centres'. The phrase 'in the presence' was omitted".

JOACHIM JUNGE (1587–1657)

A FORGOTTEN GENIUS

THE name of Junge, known also as Jung or Jungius, is to be found in few biographical dictionaries, and is seldom mentioned by historians of science. Nevertheless, his contribution to scientific thought and knowledge was significant and considerable. He lived at a time when alchemy became chemistry, astrology gave way to astronomy, and other sciences assumed a new appearance as the old scholastic approach to learning was replaced by a return to the use of experimental methods. Junge published little or nothing during his life-time, and for that reason his work has been overshadowed by that of his contemporaries. To-day, after a lapse of three centuries, his achievement is beginning to receive a well-merited recognition.

The main events of his career may be summarized as follows. Born at Lübeck in 1587, the son of a schoolmaster who died while his son was still a child, he was enabled, by the sacrifice and wisdom of a far-seeing mother, to enrol as a student at Rostock in 1606, and then at Giessen, where his brilliant intellect became so obvious that he was offered, and accepted, the chair of mathematics. This academic position did not afford him the scope for wider study which he desired, and in 1614 he resigned, and went to study medicine at Padua, where he graduated M.D. in 1618. On his return to Rostock he hoped to found an academy of sciences, and although he did succeed in establishing the Societas Ereunetica in 1622, one of the earliest societies of its kind, it survived for only two years. The reason of this failure was that Junge was suspected, though quite unjustly, of being a Rosicrucian, a member of the secret society of that time devoted to astrology. It was not surprising, however, that the progressive views of Junge, which included his advocacy of teaching in the vernacular, and of a greater use of experiment, brought him into disrepute with the Church. As a result of this misfortune, and the threat of an accusation of heresy, he removed to Hamburg, where he passed the last thirty years of his life as rector of the High School, and where he died on September 23, 1657.

Junge's opinions won the approval of Leibniz, who placed him on a level with Galileo, Kepler and Descartes, while Goethe said that if the methods of Junge had been followed sooner, the advance of human knowledge might have been hastened by a century. Unappreciated in his life-time, his service to science remained obscure. Like his contemporary, William Harvey, he lost many of his manuscripts in a fire, and the suspicion with which he was surrounded prevented the publication of those that remained. Unlike Harvey, Junge did not live to see the result of his labours. His disciples and followers recognized their merit, however, and among his works, printed during the century following his death, are "De plantis Doxoscopiae physicae minores" (1662), "Isagoge phytoscopia" (1678), "Logica Hamburgensis" (1681), "Geometrica empurica" (1688), and "Opuscula physica botanica" (1747).

Most of those books have become very rare, but during the succeeding years his memory has been kept alive by his admirers, and especially by those in Hamburg. On the 300th birthday of Junge in 1887, Dr. Konrad Friedlander reported that "in terms of the will of Joachim Jungius, about 500 scholarships had been awarded, for the furtherance of scientific work, and that the list of scholars included many distinguished persons". In 1928, Prof. Meyer-Abich, of the University of Hamburg, founded the "Jungius Kommission", with the view of investigating the unpublished manuscripts, and in the following year a commemorative volume was printed, entitled "Beitrage zur Jungius-Forschung". Eventually, in 1947, a "Joachim Jungius Gesellschaft" was inaugurated in Hamburg, with the wider object of "promoting research in all branches of science, and extending the scope of scientific work".

The year 1957, the tercentenary of his death, marked a further revival of interest. Dr. J. H. S. Green paid a graceful tribute to the memory of Junge in an article in *Nature* (180, 570; 1957), and when the Joachim Jungius Gesellschaft met at Hamburg on October 31, 1957, under the presidency of Prof. Kurt Heyns, his first duty was to award a Joachim Jungius Prize and Medal to its first recipient, Prof. Rudolf Meyer, of Zurich, who has long been an ardent student of the works of Junge, and had recently edited a new edition of "Logica Hamburgensis". Prof. Meyer than delivered an address on "Joachim Jungius and the Philosophy of his Time", which, following the introductory remarks of the president, is printed, with other noteworthy papers by various authorities, in the little volume commemorating the occasion, which bears the title "Die Entfaltung der Wissenschaft" (The Development of Science)*, and which may be read with pleasure and profit by every scientist, whatever be his special branch.

Prof. Kurt Vogel deals with "Mathematics in the Early Years of the Seventeenth Century". Prof. R. Hooykaas, of Amsterdam, in a paper on the knowledge of elements and atoms at that time, shows how Junge championed the atomic theory, and opposed the older philosophy, alleging that in spite of chemical changes, atoms retained their individuality. This paper concludes with the significant remark that "one free man can do more for science than a whole crowd of *Konformisten*". The important place of Junge in the history of botany is clearly revealed by Prof. Walther Mevius, who tells us that Junge's contribution to that science was probably his greatest achievement. He was indeed one of the founders of scientific botany, and to him we owe the terminology which was perfected later by Ray and Linnæus. Junge was the first to classify plants according to the varieties of their component parts. Many modern terms are of his coinage, and, as Charles Singer stated in his "Short

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* Die Entfaltung der Wissenschaft: Zum Gedenken an Joachim Jungius (1587–1657). (Vorträge gehalten auf der Tagung der Joachim Jungius-Gesellschaft der Wissenschaften, Hamburg, am 31 Oktober/1 November 1957 aus Anlass der 300 Wiederkehr des Todestages von Joachim Jungius.) Pp. 160. (Glückstadt: Kommissions-Verlag J. J. Augustin, 1958.)

History of Biology", Junge "had a real insight for classification, grouping plants according to the formation of their flowers, and naming the groups Compositae, Labiatae and Leguminosae", names which still remain. The paper which follows, on "Experiment in the Medicine of the Seventeenth Century", gives an interesting account of this important epoch in medical history, and is contributed by Prof. J. Steudel, of Bonn. It is illustrated by eleven figures, showing some experiments of Harvey, de Graaf, Boyle, Mayow and others. Prof. W. Flitner, of Hamburg, describes the logic and philosophy of the period, and his colleague, Prof. D. K. Deitrich Schmidt, discusses the changing outlook of theology in the days of Junge.

The scope of this excellent collection of monographs is extended even more widely by a thoughtful and suggestive study by Prof. Karl Bauch, Freiburg, of the new approach to art, adopted by Raphael, Rubens and other artists in the opening years of the century under review. Twelve illustrations in this paper are of much interest. Finally, an appropriate background to the whole scene is provided by Prof. Otto Brunner in an essay on "Hamburg's Historical Position during the Lifetime of Joachim Jungius". This article, also appropriately illustrated, should prove valuable as a reference to the contemporary topography of the city. Too often, in writing of the history of science, this essential basis of social history is omitted. The Joachim Jungius Society is to be warmly congratulated on the publication of this timely and attractive little volume, which not only pays a fitting tribute to the work of a forgotten genius but also builds upon that work an edifice well worthy of so sound a foundation.

DOUGLAS GUTHRIE

EDUCATION IN THE AGE OF SCIENCE

IN a recent issue of *Daedalus* (88, No. 1 ; 1959), ten distinguished American correspondents examine different aspects of American education and their place in a rapidly evolving scientific and technological age. The articles are grouped in five pairs, each pair representing two different points of view regarding the same aspect of education. The problem of Prof. Sidney Hook and George N. Shuster is that of the general nature and ends of education. Prof. Hook holds that the ends are threefold : to produce skills, knowledge and loyalties. On all three aspects there is a difference of opinion. If 'skills' mean the ability to think, speak and write effectively, education must clearly aim at such skills ; but do they include skills of everyday living ? Here there are rigorists and latitudinarians. Regarding knowledge and loyalties, the differences go deeper. Prof. Hook is a secularist who believes that the only knowledge worthy of the name is that which is accredited by scientific method, and that even moral judgments are subject to empirical tests. Shuster believes that theology is the queen of the sciences, and that the most sure and important knowledge has another kind of certification altogether.

In the papers of the second group, Prof. Douglas Bush states the case for the humanities in education, and Prof. Ernest Nagel the case for the sciences. Both advocates recognize that both disciplines are essential but they differ about two points. Prof. Bush, concerned about the 'sophisticated vulgarity' of newspapers, best-sellers, radio, advertising and music, thinks that much of this is a by-product of science, partly through its technical applications, partly through the exaltation of science in the popular mind. Science has made 'mass civilization' possible, and 'the religion of commonness' that has resulted has been creeping out from news-stands and films into the schools and universities. Science provides the means by which a commercial civilization may exploit the mind more expertly, but no corresponding resistances against the shoddiness of mass values ; nor does it do anything to prevent the 'spiritual impoverishment of the expert' himself.

Prof. Nagel, admitting the part of science in helping to produce mass culture, replies that it is unjust to make science responsible for men's misuses of it, and argues that our mass culture, for all its defects, represents a high-water mark in democratic education. He then makes a claim for science that provides a second bone of contention, believing that scientific method, taken broadly as the method by which propositions are validated, is the sole and sufficient means of establishing any kind of knowledge. The judgments of value passed by a humanist upon poetry or music may be merely expressions of his feeling ; but if they say more than that, if they offer themselves as true, there is only one way of establishing them, and that is the approved way of science. Bush, Shuster and others do not agree. They hold that the poet, the religious man, and the critic have insights that such a method is inadequate to appraise. Here, as elsewhere, it becomes clear how difficult it is to talk about education without entering into philosophy.

The chief issue of the third group is raised by Prof. Arthur Bestor's contention that American schools are trying to do too much. If all three ends —skills, loyalties and intellectual discipline—are important, can a school sensibly try to achieve all of them ? Perhaps a residential school can, since it has full control of the pupil's time. A day school cannot ; if, with a few hours a day at its disposal, it tries to take over the functions once performed by home, church and work, as well as to discipline the young mind, it will do all of them badly. Prof. Bestor's proposal for American schools is clear-cut : let them realize that they are over-extending themselves and close their ranks, so that they can perform their own function well—that function being distinctively intellectual. To maintain their standards in the face of local pressures, they should set up State-wide systems of examination, which would free the able students from the educational 'lock step' and would test actual achievement rather than accumulations of credits and hours.

Prof. Bestor's views are challenged at several points by Prof. John L. Childs, who argues that the sensitivity of American schools to the social needs of their pupils is an advantage, not a weakness, and that the schools are not to be improved by a return to the narrow intellectualism of the French and other systems.

The issue raised by the two papers in the fourth group is : What can the schools do to prepare their students for the sort of citizenship demanded by the United States' new place in the world ? Dr. Reinhold Niebuhr tries to make this new place clear. It is one in which three new conditions prevail : America has become the acknowledged leader of the free world ; is faced with a powerful and resolute rival ; and must apparently live with a 'nuclear stalemate'. In this precarious position, technology is no doubt important ; but Dr. Niebuhr thinks that an understanding of Russian imperialism and the curious American 'anti-imperialist imperialism' is equally so. It is necessary to have representatives abroad who speak the languages and understand the cultures of those among whom they are living ; and though there is no study that will enable one to forecast the future, the study that does most to equip one for understanding the larger problems of the day is history.

Hans Morgenthau puts his emphasis in a different place. Agreeing that history is important, he thinks it could best be taught and understood not as a string of events but as the exemplification of principle, and above all, the principle that nations seek power. A thorough grasp of this principle, as exemplified historically, would throw more light on the present scene than any study of the events or personalities of the day.

The fifth group of articles examines the social matrix within which education in the United States operates. Prof. Margaret Mead looks into the reasons for the separation between the world of the scientist and that of his intended audience, the general population. In this way she points to the mechanism that may be responsible for the widening of the gap between the intellectual and society at large. Prof. David Riesman directs attention to the medium in which the academic himself grows and moves—lest educators seek the sources of their difficulties only outside the sphere of their own organizational setting.

Most of the papers have been edited by Prof. Brand Blanshard, who has also contributed an introduction to them. For background, this special issue of *Daedalus* also contains a reprint of A. N. Whitehead's famous essay on "The Aims of Education", which was first written some forty years ago. For those concerned with education, this essay may serve the purpose of periodic re-dedication as well as any other source.

PUBLIC LIBRARIES IN ENGLAND AND WALES

THE report of the Committee appointed by the Minister of Education in September 1957 to consider the structure of the public library service in England and Wales* reviews briefly the development of the public library service and the changing views of its functions, particularly the changes in formal structure since the Kenyon Committee reported in 1927. Turning then to the public library service to-day, it suggests that three main questions arise : how a really adequate service throughout the country can best be provided ; the standards for judging the efficiency of a library service ; and the requisite conditions which will enable a local authority to provide an efficient service. Chapters on the future structure of public library administration, library co-operation, staff and premises, the position in Wales, library charges and library legislation follow.

The principal recommendations are that the Minister of Education, assisted by two advisory bodies for England and Wales, respectively, should exercise a general responsibility for the public library service, with powers to enforce the discharge of its statutory duty by any library authority he considers to be in default. Every public library authority should have a statutory duty to provide an efficient library service, and the minimum annual expenditure on the purchase of books expected from a non-county borough or urban district council as an independent library authority should be £5,000 or 2*s*. per head of the population. All library authorities should be given powers to appoint library committees directly responsible to the councils.

The existing regional committees should be given statutory recognition and required, under schemes approved by the Minister, to provide a satisfactory system of library co-operation within their regions and to work in conjunction with the National Central Library. The local authorities should contribute substantially to the cost of the National Central Library, with greater representation on its governing body and in its administration. An adequate series of regional catalogues and the catalogue at the National Central Library should be completed as a matter of urgency and with a non-recurrent Treasury grant. Extra-district charges should be abolished for readers using libraries outside their own areas. Salary scales for the staff of public libraries should be commensurate with their qualifications and responsibilities and so applied as to make career prospects attractive. To meet the need for considerable improvement in public library premises and for many new library buildings a higher priority should be given to capital expenditure for this purpose. No charge should be made to borrowers of books or other material except for notification that the book or material is available or for retention beyond a prescribed period, and legislative provision should be made authorizing the levying of these charges by library authorities.

A new Public Libraries Act should be passed to give effect, so far as is necessary, to these recommendations and giving all library authorities specific powers to combine or co-operate with each other, and with education and other authorities, to provide lectures and cultural activities, to provide and lend such material as gramophone records and films and to acquire land compulsorily for library purposes under the Act. It is also recommended that the position of local authorities responsible for museum and art galleries should be considered, since it may be necessary to legislate separately for libraries, museums and art galleries in future. A minority report by Mr. J. Bulman and Mr. S. J. Skillen enters reservations as to the type of local authority which should become or remain library authorities and dissents from the suggestion as to a minimum expenditure on books.

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* Ministry of Education. The Structure of the Public Library Service in England and Wales : Report of the Committee appointed by the Ministry of Education in September 1957. Pp. iv+57. (Cmnd. 660.) (London : H.M. Stationery Office, 1959.) 3*s*. 6*d*. net.

THE NATURE OF COAL

A SYMPOSIUM on the nature of coal was held at the Central Fuel Research Institute, Bihar, during February 7–9. The delegates were welcomed by Dr. A. Lahiri, director of the Institute, and by Prof. M. S. Thacker, director-general of scientific and industrial research in India, who referred to the valuable work already done by the Institute and to the need for symposia to review progress and exchange ideas. Dr. B. C. Guha of University College, Calcutta, gave the inaugural address. Coal, he said, was the parent of the industrial revolution and our principal source of heat and power. With the advent of atomic energy, some people feel that the use of coal as a fuel will decrease. Even if this were true, however, coal will still remain the source of numerous organic compounds—dyes, drugs, plastics and explosives. After less than a century of research on coal there remains much to be learnt and, no doubt, many new materials and processes to be developed.

The main subjects of the symposium were the origin and formation of coal; petrographic studies; X-ray structure; the constitution of coal as revealed by physical methods or by chemical methods; and the physico-chemical properties of coal. Contributions were received from a number of foreign countries, including Great Britain, the U.S.S.R., Japan, the United States, Canada, Australia, New Zealand, Czechoslovakia, Belgium, and West Germany.

In the session dealing with the origin and systematics of coal, the opening paper, by Dr. A. Lahiri, was on the metamorphism of coal, that is to say, on the transformation of vegetable matter and peat to lignite, bituminous coal and anthracite. This is referred to again later. In addition, there were interesting contributions from certain Russian investigators, namely, W. Rakovsky on the processes of formation of fuels and ways of solving the general problem of genesis, N. M. Karavayev on the early stages of formation of fossil fuel, A. Z. Yurovsky on the theory of the origin of sulphur in coals, V. S. Veselovsky on the chemical nature of caustobioliths from the point of view of genesis, and V. I. Kassatochkin on the physico-chemical aspects of the metamorphism of coals. There was also a well-discussed paper by A. Gillet and P. Colson on petroleum and anthracite from cellulose. Prof. Gillet, in presenting this paper, first dealt with the earlier work on the subject and later expounded his theories of the development of the main liquid and solid fuels from cellulose, employing numerous diagrams for illustration.

In the following session, papers were presented on petrographic studies on Indian coals and their relation to certain chemical properties, the significance of X-ray studies in the elucidation of problems of coal formation, deductions from recent X-ray data on coals, X-ray studies on oxidized coals and humic acids. On the ultra-fine structure of coal, the contributions were made on the sorption properties and structure, on the relation between internal surface and functional group measurements, on the adsorption of krypton by coal, and on the porosity of coal and of carbonized products as revealed by densities using helium and mercury as the displaced liquid. Considerable interest was shown in 'heat of wetting' and in the significance of the results obtained by different methods of determination.

In the papers and discussions on physical methods of studying the constitution of coals, the nine steps of Seyler did not receive support from T. N. Basu and D. Bagchi in their work on reflectance. Definite changes of reflectance, however, were confirmed at 85 per cent carbon and at 90–91 per cent carbon. Indeed, the changes when the carbon of coal exceeds 85 per cent were noted by many contributors from different sources. These changes are reflected in natural moisture, density, calorific value, oxygen, and coking properties, and seem to be related broadly to the elimination of hydroxyl groups in a drastic and abrupt manner involving re-orientation of molecular structure, probably with formation of quinone linkages. In India the mine dusts from such coals (85 per cent carbon) seem particularly dangerous in respect of mine explosions.

J. D. Brooks (Australia) presented a useful review of the principal chemical methods of investigating the constitution of coals, covering the results obtained by the various methods of determining functional groups, oxidation reactions, hydrogenation, hydrogenolysis, sulphonation, hydrolysis and pyrolysis of coals. J. B. Stott (New Zealand) dealt with the effects of evaporation on the early stage of spontaneous combustion of coal. Problems of coal heating have often presented baffling inconsistencies in the past: many of these could probably be explained by the influence of evaporation of water.

L. D. Ahuja and others, in discussing the conversion of non-coking coal to coking coal by partial hydrogenation, considered that the improvement in coking property is largely bound up with the removal of the more stable oxygen linkages. Drs. P. N. Mukherjee and A. Lahiri, dealing with the constitution of humic acids, pointed out that, on the basis of X-ray and infra-red studies, there is a close similarity between the structural units of coal and humic acids. From studies of various properties, including ultimate composition, molecular weight, equivalent weight and the distribution of functional groups, a tentative structural model was suggested for humic acids.

M. S. Iyengar and others claimed that with high-sulphur coals (up to 6 per cent organic sulphur) there are three different types of sulphur, namely: (1) sulphur eliminated during the initial stages of oxidation; (2) sulphur oxidized to sulphonic acids; and (3) sulphur resistant to oxidation. The first type has not been identified, the second has been identified as thiophenol, while the third is tentatively assumed to be thiophene.

A striking paper was given by B. K. Mazumdar and his colleagues on dehydrogenation studies carried out on several coals of different rank, on vitrains, on oxidized and weathered coals, and on coal extracts and pitch. They had used Vesterberg's technique. The optimum temperature for dehydrogenation with sulphur was found to be 200°–360° C. for bituminous coals and lignites. (Anthracite reacts with sulphur only above 480° C.) The hydrogen sulphide evolved accounts for more than 92 per cent of the products of reaction, but small amounts of methane are also detected. Dehydrogenation under these conditions was ascribed primarily to the presence of alicyclic (hydro aromatic) structures, and the amount present was measured by the hydrogen sulphide formed. This was confirmed by a hydrogen balance of the coal and its dehydrogenated products. It was shown that 'alicyclicity' progressively diminished with rank, from 25 per cent in lignite to almost nil in anthracite. Similarly, alicyclicity with respect to hydrogen (Hal/H) varied from 60 per cent in lignite to nil in anthracite.

Further dehydrogenation of coal resulted in complete destruction of coking properties, inhibition of the formation of tar, and higher yields of char—apparently at the expense of the tar bodies. The yield of low-temperature tar was found to be proportional to (and also nearly equal to) the alicyclic carbon in coal.

Prior dehydrogenation led to the retention of 90 per cent of the original carbon of coal in low-temperature carbonization char, whether employing lignites or bituminous coals, whereas in normal (high-temperature) carbonization only 70–80 per cent of the carbon of the same coals was retained. The 'extra' carbon retained as a result of dehydrogenation and subsequent pyrolysis was considered to be a measure of the alicyclic carbon and hence of alicyclic hydrogen. A simple test of volatile matter in the presence of sulphur or selenium would afford a direct estimate of the alicyclic carbon retained in the char.

B. K. Mazumdar and his colleagues also explained the influence of the alicyclic component on the behaviour of coal in coking and tar formation, spontaneous combustion and weathering. Knowledge of the alicyclicity of coal enabled one to compute the aliphaticity, which was practically constant for all coals at 9–10 per cent of the carbon.

In a paper on aliphatic hydrogen in coal, J. N. Bhowmick and his collaborators described experiments employing chlorination to determine the aliphatic groups. Exhaustive chlorination of the coal at 200° C. was followed by hydrolysis in potassium hydroxide solution, and on the basis of the estimation of the functional groups formed in the hydrolysed products, as well as the loss of carbon sustained during chlorination, the distribution of aliphatic groups in coals of different ranks was worked out.

F. Kaiser, H. S. Rao and A. Lahiri, reporting on the disposition of methyl groups, described work in which they first formed an estimate of the side-chains in coal by the application of Kuhn–Roth's procedure for the determination of $C\text{–}CH_3$ groups. (The method depends on the fact that every side-chain contains one, and only one, methyl group, and that every methyl group can exist only as the terminal carbon of a side-chain.) The variation of $C\text{–}CH_3$ content with increase in rank was studied, and a free radical mechanism postulated for the coalification process. The mechanism attempts to explain two important facts associated with the metamorphism of coal, namely, the increase in aromaticity and the evolution of methane during the coalification process.

Dealing with pyrolysis and its relation to the structural parameters of coal, B. K. Mazumdar, S. K. Chakrabartty and A. Lahiri showed how, on a basis of recent knowledge obtained from X-ray and infra-red studies on carbonized coal (and in the light of oxidation and dehydrogenation studies on coal and its carbonized products), a mechanism could be worked out for the pyrolysis of coal up to 600° C. Low-temperature (600° C.) coke or char, they claimed, is entirely aromatic in character and no aromatic carbon of coal is lost by carbonization at 600° C. The primary bodies of tar come mainly from the alicyclic component, whereas the hydrocarbon gases come from the aliphatic structures. Correlation was shown to exist between the yield of gas and aliphaticity.

N. Berkowitz, in dealing with the decomposition and diffusion processes in coal pyrolysis, claimed that the classical interpretation attached to the weight-loss – temperature curve (namely, that it indicates a slow and extended chemical decomposition) is at variance with experimental facts. Such curves, if interpreted in the light of a diffusion process, offer material from which several important conclusions about the nature and kinetics of the pyrolytic processes can be drawn.

The broad picture that emerged from the papers and discussions was that coal can be regarded as essentially a binary mixture of aromatics dispersed in non-aromatics via carboxyl groups. Fusain (long attributed to forest fires) was probably one of the primary stages in coal formation.

Summarizing and following Lahiri on the metamorphism of coal, the general trend in the changes from peat to lignite, and bituminous coals, is primarily one of dehydration. At certain stages this dehydration seems to occur in discrete steps, notably at about 70, 85 and 91 per cent carbon. With increasing enrichment in carbon there is a diminution in the water-holding capacity of the material, representing a change from 'sol' to 'gel'. At the lignite stage there occurs an increase in hydroxyl groups, both alcoholic and phenolic, with some carboxyl groups, but quinone and carbonyl groups are relatively scarce. Some of the coal carbon—about 20 per cent—is present as alicyclic compounds, but about 60 per cent is in the form of aromatic compounds. This complex colloidal gel in lignite is still dispersed in water. The dispersing phase (water) is not merely absorbed physically in pores or micropores, but is largely held to the organic mass by chemisorption or hydrogen bonding and polar absorption. When the moisture falls to 15 per cent or so, the sub-bituminous or ligno-bituminous stage is reached, but the alicyclicity and aromaticity are largely unaffected. The oxygen and moisture in the dispersed phase are reduced, largely through dehydroxylation and decarboxylation, but dehydroxylation still continues up to 84–85 per cent carbon. Here, however, there is a marked change in capacity moisture and coking properties, reflected in changes of hardness, elasticity, calorific value and resistance to weathering. The reflectance and refractive index are also increased: alicyclic carbon increases, and also the yield of tar. Thus, the sol-to-gel transformation is complete and the stage of true bituminous coking coals reached. Under X-ray diffraction the structure of the coal showed an apparent emergence of order from previous disorder, but there is no definite evidence of any appreciable increase in the number of rings (averaging 4 or 5): the aromatic nucleus does not grow, although the coal becomes predominantly aromatic. Alicyclic carbon falls to 10 per cent of the coal, but is of great value in providing the 'coking constituents' of Bone and Fischer. Coking coals consist of aromatic ring structures dispersed in alicyclic carbon structures. In Nature such changes are apparently brought about by high tectonic pressures with considerable evolution of methane, especially when the carbon rises from 85 to 87 per cent.

Finally, in anthracites, the 'ordered' carbon is involved: there is an abrupt rise in reflectance and in aromaticity, with changes in general appearance including the elimination of banding and petrographic heterogeneity. Coking properties are destroyed, and there is a small but definite rise in moisture content. The hydrogen content falls by 25–50 per cent of its earlier value. Apparently the organic gel has been transformed into an organic crystalloid. The process is thus primarily dehydration followed by decarboxylation, dehydroxylation and demethylation. The original aromatic carbon groups are not much affected by geochemical and geological changes until the 91 per cent carbon rank is reached. It is the variations in the alicyclic and aliphatic bodies which are largely responsible for the different types of coal, especially of bituminous coal.

The proceedings of the symposium are to be published in book-form.

J. W. WHITAKER

ROLE OF POLY-β-HYDROXYBUTYRIC ACID IN THE ASSIMILATION OF ORGANIC CARBON BY BACTERIA

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IN 1936, Barker[1] observed that resting cells of a colourless alga, *Prototheca zopfii*, assimilate a large fraction of the carbon of the organic substrates which they oxidize. The same phenomenon was soon shown to occur in bacteria[2,3], and for some years the study of 'oxidative assimilation' had a considerable vogue among bacterial physiologists. The relevant literature has been reviewed by Clifton[4]. The discovery of the nature of bacterial photosynthesis by van Niel[5] in 1931 was followed by studies on the photosynthetic metabolism of organic substrates by the purple bacteria, which showed that under anaerobic conditions in the light these organisms can perform a very effective assimilation of organic carbon[6–8].

The work which has been done on the oxidative and photosynthetic assimilation of organic compounds by bacteria has thrown little light on the mechanism of the process. A dependence on the simultaneous formation of adenosine triphosphate is indicated by the observation that uncouplers of oxidative phosphorylation such as 2,4-dinitrophenol may prevent oxidative assimilation at levels which do not diminish the rate of respiration. From a study of the oxidative metabolism of specifically labelled radioactive substrates by *Pseudomonas saccharophila*, Wiame and Doudoroff[9] concluded that acetyl fragments are the intracellular metabolites that undergo assimilation.

It is furthermore evident that assimilation is not necessarily coupled with general cellular synthesis and growth, since bacteria can assimilate organic carbon with unimpaired efficiency in the absence of a nitrogen source. Under these conditions, the flow of carbon into the nitrogenous constituents of the cell must be negligible, and it could therefore be expected that the assimilated carbon accumulates in a limited group of cell materials. The evidence on this question is scanty and not clear. Gaffron, who first studied the photosynthetic assimilation of organic compounds by resting cells of purple bacteria[6,7], postulated the existence of a primary assimilatory product with the empirical formula $(C_4H_6O_2)_n$, and succeeded in isolating small quantities of a polymeric substance with this elementary composition from cultures grown photosynthetically on butyrate. Further pursuit of this lead seems to have been discouraged by van Niel's report[10] that the gross composition of the cells of purple bacteria corresponds closely to the composition of Gaffron's postulated assimilatory product, and the problem has remained where Gaffron left it in 1935. Inconclusive results have been obtained in the search for products of oxidative assimilation by resting bacteria. Wiame and Doudoroff[9] were unable to identify the radioactive cell-constituents formed by *Pseudomonas saccharophila* at the expense of substrates labelled with carbon-14, and suggested tentatively that the assimilated carbon flowed into many different cell materials, including proteins. Recently a similar conclusion was reached by Morita[11], who studied the dark oxidative assimilation of acetate, labelled with carbon-14, by *Rhodopseudomonas palustris*.

In 1927, Lemoigne[12] discovered that a polyester of β-hydroxybutyric acid is a major component of the cells of *Bacillus megaterium*, and the same substance was later found in other *Bacillus* species[13]. There is a considerable literature on the properties and metabolic behaviour of poly-β-hydroxybutyric acid in the genus *Bacillus*[12–20], and the accumulated evidence suggests that it functions as an intracellular reserve of carbon and energy for these bacteria. The recent observations of Macrae and Wilkinson[20] provide particularly convincing support for this hypothesis. The possible relevance of the investigations on poly-β-hydroxybutyric acid to the more general problem of bacterial oxidative and photosynthetic assimilation has been overlooked, no doubt because this polymer appeared until recently to be confined to a few species of bacteria. It was found in *Azotobacter* many years ago[21]; but its widespread occurrence in Gram-negative bacteria was first demonstrated in 1958 [22]. It has not been detected in any other group of micro-organisms, or in higher plants and animals.

The observation by our colleague Dr. Germaine Cohen-Bazire that purple bacteria accumulate massive quantities of poly-β-hydroxybutyric acid during photosynthetic growth on certain organic substrates prompted us to investigate its role in bacterial assimilation. We have examined the products of oxidative assimilation from glucose, acetate and butyrate in *Pseudomonas saccharophila*, and of photosynthetic assimilation from acetate and butyrate in *Rhodospirillum rubrum*. In all cases, a major fraction of the assimilated carbon (60–90 per cent) initially accumulates within the cell as poly-β-hydroxybutyric acid; when the external substrate is removed, there is a fairly rapid intracellular breakdown of the stored polymer. These observations suggest that poly-β-hydroxybutyric acid may have a general physiological function in bacteria as a primary product of carbon assimilation, its role in bacterial metabolism being analogous to that of

Table 1. PHOTO-ASSIMILATION OF LABELLED ACETATE AND BUTYRATE BY *Rhodospirillum rubrum*

	Substrate			
	0·01 *M* acetate		0·002 *M* butyrate	
	Cells	Polymer fraction	Cells	Polymer fraction
Initial dry weight (mgm.)	1,000	16	1,000	5
Increase in dry weight (mgm.)	585	329	260	130
Increase in polymer carbon* (mgm. C)		184		73
^{14}C incorporated (mgm. C)	248	173	100	58

* Calculated for $(C_4H_6O_2)_n$ from the increase in dry weight.

starch and glycogen in the metabolism of other organisms. Past failures to discover the polymer in bacteria (such as *P. saccharophila*) where it is a major component of the cell are readily understandable in view of its chemical properties. It represents a type of cellular constituent which is not detectable by the standard analytical procedures used for the fractionation of cell materials. Applied to cells which contain the polymer, these standard procedures result in the inclusion of the polymer with the protein fraction.

Isolation and Estimation of Poly-β-hydroxybutyric Acid

The poly-β-hydroxybutyric acid synthesized by *P. saccharophila* and *R. rubrum* is contained in sudanophilic cytoplasmic granules, similar to those of *Bacillus megaterium*[19]. These granules were isolated by digestion of the cells with alkaline hypochlorite[19], sedimented by centrifugation and washed with water. They were then treated with acetone and ether in order to remove lipids, after which the poly-β-hydroxybutyric acid was extracted with chloroform, dried and weighed. Such material is designated as 'polymer fraction' in the experiments described below. The poly-β-hydroxybutyric acid from each species was further purified by fractional precipitation from chloroform extracts with acetone/ether (2 : 1, v/v). The solubility properties, melting point and infra-red spectrum of the polymer from *P. saccharophila* and *R. rubrum* agree with those of the polymer from *Bacillus* spp.

Metabolic Role of Poly-β-hydroxybutyric Acid in *R. rubrum*

Polymer formation by *R. rubrum* at the expense of uniformly labelled acetate and butyrate was investigated. Cultures were grown at 30° C. in the light in Hutner basal medium[33] supplemented with either 0·01 *M* acetate or 0·005 *M* butyrate, and continuously aerated with 95 per cent nitrogen–5 per cent carbon dioxide. The cells were harvested by centrifugation, resuspended in Hutner phosphate buffer[24], and maintained in the light at 30° C. in a continuous stream of 95 per cent nitrogen to 5 per cent carbon dioxide for 12–16 hr., in order to deplete the internal polymer store. An initial sample was then taken, radioactive substrate was introduced, and the aeration mixture was changed to 95 per cent helium–5 per cent carbon dioxide in order to prevent nitrogen fixation. When most of the radioactive substrate had disappeared from the suspending medium, the cells were harvested by centrifugation, washed and resuspended in a small volume of distilled water. Dry weights of cells and polymer were measured on initial and final samples, and radioactivities on the final sample. The results are shown in Table 1. For ease of comparison, the actual data have been recalculated on the basis of an initial dry weight of cells of 1,000 mgm. In the experiment on acetate assimilation, the cellular dry weight increased by 594 mgm., and the polymer fraction accounted for 329 mgm. of this increase. The quantity of polymer carbon in the cells increased by 184 mgm., and the weight of carbon-14 incorporated from acetate in the polymer fraction was 174 mgm. From this it follows that acetate carbon flows into polymer without appreciable dilution, either by pre-existing cellular carbon, or by fixation of carbon dioxide. The experiment on assimilation of butyrate gave similar results; but somewhat less of the assimilated butyrate carbon was incorporated in polymer (58 per cent of the total, in contrast to nearly 70 per cent of the total in the case of acetate), and the dilution of radioactivity was appreciably greater.

The cells which had become radioactive as a result of assimilating labelled acetate or labelled butyrate were used for experiments on the subsequent fate of the polymer. The washed cells were resuspended in Hutner phosphate buffer supplemented with 0·1 per cent ammonium chloride, and illuminated for 12 hr. without an exogenous organic carbon source in a constant stream of 95 per cent nitrogen and 5 per cent carbon dioxide. Additional aliquots of the cells labelled from butyrate-^{14}C were similarly treated, but were furnished with an exogenous organic carbon source (either butyrate or succinate). At the end of the period of illumination, the cells were harvested, and radioactivities and dry weights of the cells and the polymer fraction were again determined. The results are shown in Table 2. In the absence of an exogenous organic carbon source, more than 90 per cent of the stored polymer disappeared, but a substantial part of the carbon-14 initially present in the polymer fraction remained in the cells. This fact shows that the polymer can serve as an endogenous carbon source for the synthesis of other cell-constituents. The cells provided with an exogenous

Table 2. FATE OF POLY-β-HYDROXYBUTYRIC ACID IN *Rhodospirillum rubrum* INCUBATED ANAEROBICALLY IN THE LIGHT WITH A NITROGEN SOURCE, IN THE PRESENCE AND ABSENCE OF EXOGENOUS SUBSTRATES

Experiment No.	1		2					
Exogenous carbon source	None		None		Butyrate		Succinate	
	Cells	Polymer	Cells	Polymer	Cells	Polymer	Cells	Polymer
Initial dry wt. (mgm.)	1,000	213	1,000	108	1,000	108	1,000	108
Change in dry wt. (mgm.)	−50	−201	−91	−100	+322	+13	+377	−96
Initial ^{14}C (mgm. C)	156	110	78	46	78	46	78	46
Change in ^{14}C (mgm. C)	−48	−106	−31	−43	−17	−14	−29	−44
Net ^{14}C transfer from polymer to other cell constituents (mgm. C)	58		12		nil		15	

Exp. 1 performed with cells which had assimilated labelled acetate. Exp. 2, with cells which had assimilated labelled butyrate.

supply of butyrate increased in dry weight by about 30 per cent, and in polymer content by about 10 per cent. In this case, the loss of carbon-14 from the polymer fraction was relatively small, and almost identical with the total loss of carbon-14 from the cells. It is thus evident that the continued presence of exogenous butyrate greatly reduces the internal breakdown of polymer, and impedes its transfer to other cell-constituents. The effect of an exogenous supply of succinate is strikingly different. Under anaerobic conditions in the light, succinate is not used by *R. rubrum* for polymer synthesis, although it is an excellent substrate for growth. The cells furnished with succinate increased their dry weight by almost 40 per cent; but the succinate conferred no protection on the polymer pool, which disappeared to the same extent as in cells not furnished with an exogenous organic carbon source, and with a similar amount of transfer to other cell-constituents.

Metabolic Role of Poly-β-hydroxybutyric Acid in *P. saccharophila*

Washed cells of *P. saccharophila* strain *G* grown on mineral-glucose medium[25] were resuspended in 0·03 *M* phosphate buffer (*p*H 6·8). An initial sample was taken, uniformly labelled glucose-^{14}C at a final concentration of 0·4 per cent was added, and the suspension was shaken in air at 30° C. for 100 min. During this time, almost half the glucose was metabolized, and about 21 per cent of the glucose carbon which disappeared from the medium was incorporated in the cells. The cells were harvested and analysed as already described for *R. rubrum*. The results (Table 3) show that 66 per cent of the glucose carbon assimilated was incorporated in the polymer fraction, and that glucose flowed into polymer with very little dilution of specific activity.

Table 3. Oxidative Assimilation of Labelled Glucose by *Pseudomonas saccharophila*

	Cells	Polymer fraction
Initial dry weight (mgm.)	1,000	144
Increase in dry weight (mgm.)	193	144
Increase in polymer carbon* (mgm. C)		81
^{14}C incorporated (mgm. C)	112	74

* Calculated for $(C_6H_4O_2)_n$ from the increase in dry weight.

The assimilation of glucose observed in this experiment was much less than that customarily observed in manometric experiments, conducted with starved cells which are allowed to metabolize very small quantities of substrate[26,27]. Accordingly, a series of experiments on polymer formation under conditions comparable to those employed in the earlier manometric studies on assimilation by *P. saccharophila* were undertaken. Cells were grown on media with a mineral base, supplemented with the carbon source to be used in the subsequent experiment. They were harvested, resuspended in phosphate buffer, and shaken in air for 16 hr. at 30° C. in order to deplete their endogenous reserves. These starved cells were then permitted to oxidize a small quantity of substrate uniformly labelled with carbon-14, the course of the oxidation being followed manometrically. As soon as the uptake of oxygen indicated that substrate utilization was approaching completion, the cells were chilled to 0° C., centrifuged, washed in the cold, and resuspended in distilled water. An aliquot was used for the determination of the total radioactivity of the cells, and the remainder was digested with alkaline hypochlorite. The polymer was extracted from this digest by shaking twice with chloroform, and 10 mgm. of purified polymer was added to the chloroform extract to serve as carrier. The extract was then washed with water and evaporated to dryness. The residue was redissolved in hot chloroform, and the polymer was precipitated from this solution by the addition of an acetone–ether mixture. The amount of polymer synthesized was calculated from the radioactivity of the polymer so recovered. The results (Table 4) show that a large part of the carbon assimilated from glucose, acetate and butyrate under conditions where the efficiency of assimilation is very high is incorporated in the polymer fraction.

Table 4. Oxidative Assimilation of Small Quantities of Glucose, Acetate and Butyrate, Uniformly Labelled with Carbon-14, by Starved Cells of *Pseudomonas saccharophila*

	Substrate furnished		
	Glucose-^{14}C 5 μmoles	Acetate-^{14}C 20 μmoles	Butyrate-^{14}C 10 μmoles
Substrate metabolized, μatoms of C	24·2	38·4	33·4
Substrate assimilated by cells, μatoms of C	14·4	17·5	20·8
Substrate incorporated in polymer fraction, μatoms of C	9·2	14·4	16·7

Other tracer experiments have shown that the polymer can serve as a substrate for endogenous metabolism in *Pseudomonas saccharophila* in the absence of an exogenous carbon source. It is, however, much more slowly metabolized than in *R. rubrum* and a net transfer of polymer carbon to other cell constituents has not yet been demonstrated.

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A NEW SHORT-ACTING THIOBARBITURATE

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OF the thiobarbiturates used as intravenous anæsthetics, thiopentone, introduced in 1934, has been in recent years the most widely used. Figures for 1955 show that it was employed "in over 80 per cent of all anæsthetics in Great Britain"[1].

Unfortunately, while thiopentone produces anæsthesia of brief duration, considerable time may elapse following recovery of consciousness before the mental faculties of the patient return completely to normal, which is a disadvantage in some circumstances. Indeed, Dundee[2] states that "All out-patients who are to receive thiopentone must have the hazards explained to them beforehand and an escort for the journey home must be insisted upon. Unless arrangements are made for this escort or the patient is willing to spend the night in hospital, thiopentone should not be given".

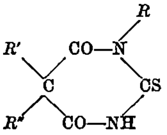
Following a suggestion made by Dr. J. G. Bourne, a search was initiated for an intravenous anæsthetic from which recovery would be more rapid than from thiopentone.

It is known[3,4] that N-alkylation of 5 : 5-disubstituted thiobarbituric acids tends to shorten the duration of action, and accordingly some 150 new N-alkyl thiobarbituric acids were synthesized.

The alkylation of 1 : 5-dialkyl thiobarbituric acids was first investigated, but this resulted in S-alkylation with the formation of the apparently unrecorded 2-alkylmercapto-1 : 5-dialkyltetrahydropyrimidine-4 : 6-diones. The required 1 : 5 : 5-trialkyl thiobarbituric acids were therefore prepared by conventional methods, for example, by the condensation of N-alkyl thioureas with either (*a*) the appropriate cyanoacetic ester (with subsequent hydrolysis) or (*b*) the appropriate malonic ester.

These compounds were examined pharmacologically by a step-wise procedure designed to screen for potency, safety and brevity. Each compound was administered intravenously to mice, and their responses were determined on the rotating drum[5]. The median effective dose (*ED*50) so found was then compared with the median lethal dose (*LD*50) to give an approximate therapeutic index. When this index permitted, the duration of action was measured at doses effective in all animals but lethal to few or none. Results of such experiments with some of these compounds are summarized in Table 1.

Table 1. POTENCY, TOXICITY AND DURATION OF SOME THIOBARBITURIC ACIDS IN MICE
Values are expressed in mgm./kgm. acid with 0·95 fiducial limits



Compound	*R'*	*R''*	*R*	*ED*50 (fiducial limits)	*LD*50 (fiducial limits)	*LD*50/*ED*50	Approximate duration at 7 × *ED*50 (sec.)
Thiopentone	1. Me–Bu^n	Et	H	5·98 (4·44–6·95)	70·25 (61·76–87·10)	12·08	3,500
Buthalitone	Bu^i	Allyl	H	17·25 (15·30–18·80)	149·9 (106·9–158·2)	8·69	20,000
B.82	Bu^i	Allyl	Me	9·57 (9·05–10·12)	81·96 (76·54–87·76)	8·56	550
B.116	Bu^i	Allyl	Pr^n	24·11 (20·09–28·92)	103·50 (96·36–111·10)	4·29	—
B.117	1. Me–Bu^n	Allyl	Bu^n	20·40 (15·42–26·99)	76·43 (61·60–94·84)	3·75$^-$	—
B.133	Bu^i	Et	Me	7·33 (6·57–7·95)	76·17 (69·76–80·98)	10·39	600
B.86	Bu^i	Et	Et	13·21 (11·59–15·07)	93·17 (86·94–99·86)	7·05$^+$	—
B.137*	Bu^i	Et	Me	7·38 (6·31–8·22)	83·60 (80·65–87·06)	11·33	550
B.135	Bu^s	Allyl	Me	6·05 (5·25–6·72)	73·38 (70·55–76·17)	12·13	450
B.80	Bu^s	Allyl	Bu^n	14·14 (10·30–19·40)	91·33 (86·60–96·32)	6·46	—
B.139	Bu^i	Pr^n	Me	11·68 (10·22–13·32)	71·06 (64·34–78·50)	6·08	—
B.158*	Bu^s	Et	Me	6·79 (5·97–7·72)	73·86 (70·30–77·82)	10·88	1,000

* Racemic stereoisomers.

From Table 1 it will be seen that the ratio *LD*50/*ED*50 falls as the size of the alkyl group on the nitrogen atom increases (for example, buthalitone, B.82, B.116; B.133, B.86; B.135, B.80). The greater brevity of B.82 compared with buthalitone illustrates the rule that methylation of the nitrogen atom tends to shorten the duration of action.

Fig. 1 illustrates the relation of dose to duration of narcosis with those compounds in Table 1 in which the index *LD*50/*ED*50 is high. With B.82 the line relating duration of action to dose remained straight even when carried into the range where some doses were lethal. With buthalitone this line turned sharply upwards long before lethal doses were reached, and higher doses gave narcosis too prolonged to be accommodated on the scale of the graph (see Table 1). The

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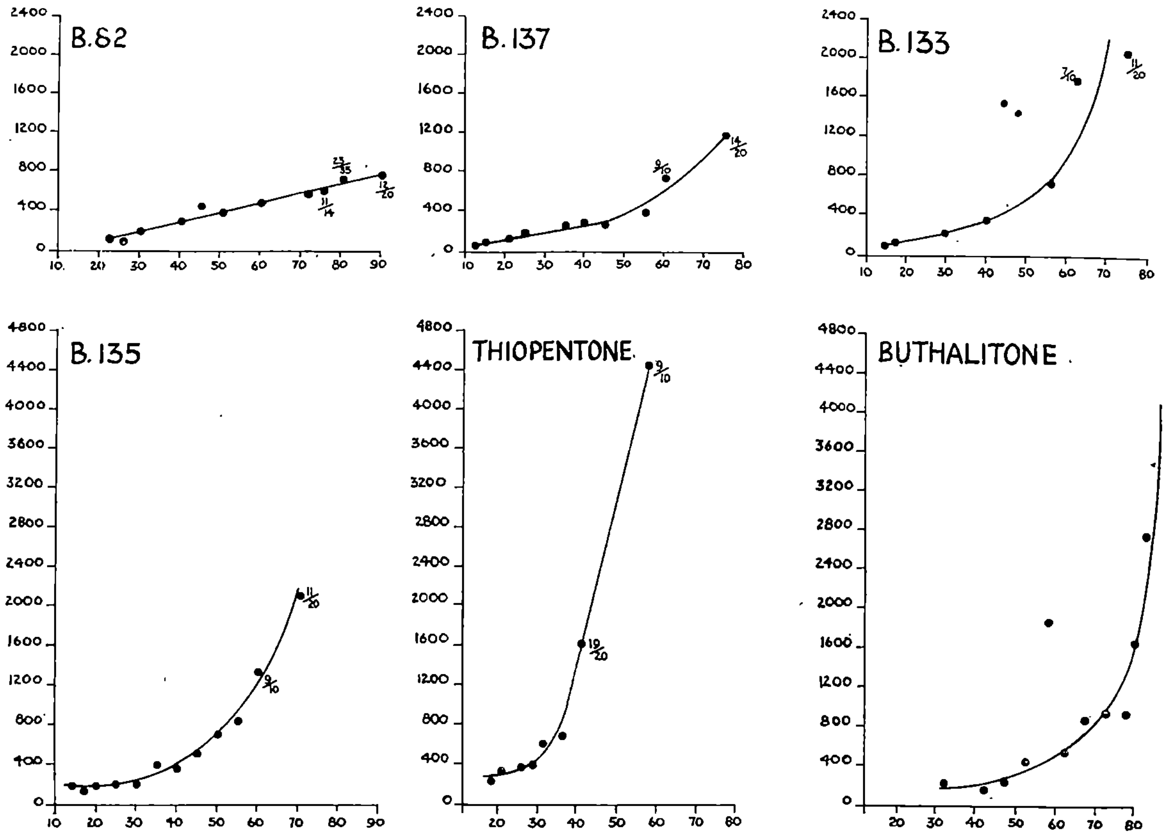

Fig. 1. Relation of dose to duration of thiobarbiturates administered intravenously to mice. All doses were effective in all mice. Where some mice died, the proportion of survivors is indicated. Ordinates, mean duration in sec.; abscissæ, intravenous dose in mgm./kgm.

curves for other compounds were intermediate in slope between those of B.82 and of buthalitone. B.158 is not included in Fig. 1, but it had a curve comparable to that of thiopentone. The flatness of the curve at high doses was taken as a favourable feature in selecting compounds for further study.

A similar procedure was adopted for selected compounds in rabbits except that loss of righting response was used instead of the rotating drum as a test of effectiveness. Some compounds were also administered intravenously to cats in order to observe the effect on blood pressure and cardiac rhythm. Compounds which possessed potency and safety comparable to thiopentone and which were considerably briefer in duration were examined by further tests, which included cumulative action and depression of respiration in rabbits, depression of ganglionic transmission in cats, local and sub-acute toxicities and duration of action after experimental liver or kidney damage in mice.

Members of the S-alkyl group had low therapeutic indices in mice and caused cardiac arrhythmias in cats. These compounds were therefore not pursued further.

The properties of three of the compounds in Table 1 (B.82, B.133 and B.137) appeared sufficiently promising in animals to warrant their preliminary investigation in man. B.82 and B.133 were soon discarded owing to the incidence of muscular tremor, sneezing or hiccough (Bourne, J. G., private communication). B.137, however, did not show these undesirable side-effects, and in a series of 71 cases receiving identical doses of either B.137 or thiopentone, no variation was observed in reactions or the time of the induction period; surgical anæsthesia was equally satisfactorily produced by either drug. Moreover, the time of recovery following administration of B.137 was approximately half that required for recovery from thiopentone (Day, D., private communication). Similar results were obtained in a smaller trial of 12 cases (Rees, L. T., private communication). Wider clinical investigations are now in progress.

The potency, toxicity and duration of B.137 in rabbits are compared with those of thiopentone in Table 2.

Table 2. Potency, Toxicity and Duration of B.137 and Thiopentone in Rabbits
Values are expressed in mgm./kgm. ± standard error

Compound	*ED*50	*LD*50	*LD*50 / *ED*50	Approximate duration at 7 × *ED*50 (sec.)
Thiopentone	2·03 ± 0·26	26·51 ± 0·42	13·06	1,200
B.137	2·12 ± 0·24	29·73 ± 0·83	14·02	700

B.137, a white crystalline solid (m.p. 96–97° C.), is the higher melting of the two possible racemic forms of 1-methyl-5-*sec*butyl-5-ethyl-thiobarbituric acid: B.158 (m.p. 56–57° C.), the other form, has been separated and also independently synthesized.

Like thiopentone, B.137 is best administered as its sodium salt, and is presented as a sterile mixture of this salt with a suitable buffer. The chemistry and pharmacology will be described in further detail elsewhere.

We thank Dr. J. G. Bourne for his valuable advice, Mr. R. T. Brittain for some experimental contributions, Miss J. Heathcote for assistance in the pharmaceutical presentation, Mr. J. J. Grimshaw for statistical analysis, Mrs. E. Nield, Miss A. Stripling and Mr. S. Ward for technical assistance, and the Directors of Allen and Hanburys, Limited, for permission to publish this work.

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AMINO-ACID COMPOSITION OF THE PROTEINS OF BARLEY LEAVES IN RELATION TO THE MINERAL NUTRITION AND AGE OF PLANTS

By DR. B. P. PLESHKOV* and DR. L. FOWDEN†

It is well known that the total nitrogen content and the relative amounts of different nitrogenous fractions of plants vary with their age and conditions of mineral nutrition. Particular attention has been paid to the free amino-acid fraction; in general the content of free amino-acids in plants increased under conditions of potassium[1–3], sulphur[4,5], calcium, magnesium and boron[6], and zinc, copper, manganese and iron[7–9] deficiencies. A similar increase results when plants are supplied with abundant nitrogen[2,10] or chlorine[11]. Nitrogen and molybdenum deficiencies caused a decrease in the free amino-acid content[2,3,8,10]. The free amino-acid content of the vegetative organs generally decreases with increasing age of the plant[5,10].

The amino-acid composition of the proteins of the vegetative organs and the changes of composition caused by different environmental factors have been studied to a lesser extent. Recent results suggest that the amino-acid composition of the proteins of the active vegetative organs is approximately constant. The investigations of Fowden showed that a close similarity exists between the composition of proteins isolated from different algae[12] and that the composition of *Chlorella* proteins does not change significantly with age[13]. Yemm and Folkes[14] did not find any significant differences between the amino-acid composition of the cytoplasmic and chloroplastic proteins of barley leaves, while Bryant and Fowden[15] detected only small differences in the amino-acid composition of the proteins extracted from daffodil leaves of different ages. This constancy of composition is not absolute, and results have been obtained indicating that the contents of individual amino-acids in the proteins isolated from sugar beet of different ages vary considerably[16]. No observations appear to exist relating plant protein composition with the conditions of mineral nutrition under which the plant developed.

The aim of the present work was to study the content of the free amino-acids and the amino-acid composition of the proteins of barley leaves of different ages grown under different nutrient conditions in respect to nitrogen, phosphorus and potassium. The barley (variety *B*-2118) was grown in sand culture in Richards's nutrient solution[17] either complete or at one-tenth dilutions in respect of nitrogen, phosphorus and potassium separately. Samples were collected 24 and 48 days after germination of the plants; the whole of the aerial portion of the plants was taken for analysis. Leaf proteins were extracted and hydrolysed by the method described earlier[15]. Free amino-acids were extracted with 80 per cent ethanol from individual plant samples, and each acid was determined quantitatively by paper chromatography[15]. Tryptophan was determined by the method of Spies and Chambers[18] (procedure K) and proline by Chinard's method[19].

The total nitrogen, protein nitrogen and amino-acid concentrations of the plants are given in Table 1. Total and protein nitrogen decreased with increasing age of plant. Considerable differences were also detected between plants receiving different treatments. Nitrogen deficiency caused a striking decrease in total and protein nitrogen; in potassium-deficient plants the total nitrogen concentration was practically unchanged, but protein nitrogen decreased markedly, especially in plants 48 days old; phosphorus deficiency also reduced the total and protein nitrogen of the plants.

In plants grown under normal nutrient conditions the total free amino-acid concentration decreased noticeably with age. All amino-acid concentrations were reduced in approximately equal proportions except those of aspartic acid and alanine, which were decreased more markedly than the rest. A slight increase in the concentration of γ-amino-butyric acid was observed. After only 24 days, nitrogen deficiency had caused a large decrease, relative to the control plants, in the concentrations of all amino-acids except tyrosine and proline. The tyrosine-level remained approximately unchanged while proline was increased three-fold. In 48-day-old nitrogen-deficient plants, total free amino-acids decreased to a still lower level. The further reduction affected mainly aspartic and glutamic acids, serine, glutamine, asparagine and proline. Only the pipecolic acid concentration

Table 1. NITROGEN AND AMINO-ACID CONTENT IN PLANTS (per cent of the dry matter)

Age of plants	Treatment	Total nitrogen	Protein nitrogen	Free amino-acids (total)
24 days	NPK	4·86	3·85	2·34
	N(1/10)PK	3·22	2·75	1·39
	P(1/10)NK	4·32	3·04	2·38
	K(1/10)NP	4·56	3·71	2·19
48 days	NPK	3·85	2·64	1·59
	N(1/10)PK	1·47	1·21	0·52
	P(1/10)NK	3·46	2·42	2·34
	K(1/10)NP	3·78	2·14	2·22

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Table 2. Amino-acid Content of the Protein Preparations
(Amino-acid nitrogen as percentage of protein nitrogen)

	24 days				48 days			
	NPK	N(1/10)PK	P(1/10)NK	K(1/10)NP	NPK	N(1/10)PK	P(1/10)NK	K(1/10)NP
Cysteine + cystine	trace*	trace*	trace*	trace*	trace*	trace*	trace*	trace*
Leucines	12·2	12·3	13·1	12·6	13·4	11·9	13·3	12·6
Arginine	13·0	13·5	13·5	13·4	11·9	11·9	9·9	10·6
Histidine	3·8	3·5	3·5	4·8	4·2	2·3	3·3	4·0
Lysine	5·3	5·6	6·0	5·3	7·6	7·1	6·0	6·3
Aspartic acid	7·1	6·2	6·9	7·1	7·2	6·9	6·1	7·6
Glutamic acid	7·5	7·6	7·5	6·3	7·0	6·7	6·0	7·0
Serine	2·9	2·7	2·9	2·5	2·4	2·9	2·1	2·5
Glycine	6·8	7·1	7·1	6·3	6·7	6·8	6·7	6·3
Threonine	3·6	3·8	3·8	3·4	3·5	3·7	2·6	2·9
Alanine	5·9	7·7	7·7	7·6	6·8	7·2	6·5	6·7
Valine	6·0	6·1	6·6	6·4	7·8	6·1	6·5	6·3
Tyrosine	2·1	2·6	3·1	2·8	3·2	3·5	2·4	3·0
Methionine	2·7	2·1	1·9	2·1	1·9	2·0	2·5	2·3
Proline	5·1	5·8	5·4	4·2	4·1	5·4	4·6	4·0
Phenylalanine	3·2	3·6	2·8	2·7	3·3	3·8	3·0	2·9
Tryptophan	1·9	1·3	1·3	1·2	1·4	1·0	1·4	1·2
Unknown amino-acid†	2	2	1	1	3	2·8	2·4	2
Amides	5·8	3·4	5·7	5·6	4·0	3·6	3·8	4·7
Total	96·9	96·9	99·8	95·3	99·4	95·6	89·1	92·9

* Less than 0·5 per cent.
† Approximate determinations.

remained unchanged when compared with control plants. Phosphorus- and potassium-deficient plants contained approximately the same total amounts of free amino-acids as control plants at the 24-day stage; at 48 days these totals remained unaltered for the deficient plants, although the level of free amino-acids in control plants had decreased. Variations in the amounts of certain individual amino-acids relative to the controls served to characterize the deficient plants. Phosphorus deficiency was associated with a decrease in the concentration of glutamic acid and a corresponding increase in glutamine, the concentration of which was five times that of normal plants at the 48-day stage. Unusually high pipecolic acid concentrations were also associated with phosphorus deficiency. Potassium deficiency was characterized mainly by a slight decrease of the concentrations of glutamic and aspartic acids relative to control plants and a marked increase in asparagine concentrations. At 48 days, one-third of the total nitrogen of the free amino-acids was in the form of this amide.

The amino-acid compositions of the protein preparations from the corresponding plants are given in Table 2. Although marked differences occurred in the total and protein nitrogen-levels of the plant tissues of different age and nutritional status, the amino-acid composition of their proteins showed distinct similarity; the values obtained for many amino-acids do not differ significantly for the various treatments if allowance is made for an experimental error of ± 5–7 per cent of the reported values. There is a trend in the proteins of older plants towards decreasing amide- and arginine-levels and slightly increased lysine contents. Nitrogen deficiency produced a definite decrease in the amide content at 24 days, and in histidine at 48 days. Smaller changes in the contents of threonine, alanine, methionine, arginine, proline and tryptophan also occurred as the nutrient conditions were varied.

Actively growing vegetative plant organs contain a large number of different enzymic proteins having different amino-acid compositions; at various stages of plant development, and under various environmental and nutritional conditions, the relative amounts of these proteins may vary widely. However, analyses of 'bulk' proteins show only their mean amino-acid composition, and real differences in concentrations of individual proteins can become masked when analyses are portrayed in terms of 'bulk' protein composition. The similarity of the amino-acid compositions determined for the proteins of plants grown under different nutrient regimes can then be still compatible with an altered balance in the complement of individual proteins.

Analysis of the barley proteins consistently revealed a new unknown amino-acid in addition to the amino-acids characteristic of proteins. The R_F of this amino-acid in butanol/acetic acid/water solvent[20] was approximately half that of cysteic acid, and so it was the slowest-moving component of the protein hydrolysate. It was only possible to detect this substance after chromatograms had been developed for at least 6 days. A few milligrams of partially purified material has been isolated, and by means of electrophoresis it has been shown to have a slightly acidic character. The values given in Table 2 for the content of this amino-acid in the protein preparations are calculated assuming a molecular weight of 75; that is, the same as glycine. The amounts of the amino-acid contained in the proteins definitely increased with the age of the plant. Isolation and identification of this amino-acid will be a problem for future investigation.

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LETTERS TO THE EDITORS

RADIOBIOLOGY

Uptake of Strontium by Pasture Plants and its Possible Significance in Relation to the Fall-out of Strontium-90

The recognition of the importance of the chain, plant–animal–man[1], in the uptake of strontium-90 by humans as a result of the fall-out of fission products made it desirable to see if species differences existed in forage plants, such that some might take up less strontium from the soil than others. This knowledge might then be used to reduce the radiostrontium content of milk, or to choose species for the reclaiming of contaminated land.

Sixteen species and strains of forage plants were grown in 1-gallon stone crocks on three different soils, similar in texture and *p*H but varying in strontium and calcium content (Table 1). Neither radioactive nor stable strontium was added to the soil, because of the difficulties of mixing and because the very small amounts of native strontium should give a better picture of the uptake of minute amounts of strontium by plants. Harvesting was carried out at eight weeks, when the plants reached the stage of incipient flowering or had reached maximum vegetative growth.

Table 1. Strontium and Calcium Content and *p*H of the Soils Used in the Experiment

Soil	Calcium (μeq./100 gm.)	Strontium (μeq./100 gm.)	Calcium/ strontium ratio	*p*H
Nord fine sandy loam	17,260	52·8	342	7·4
Yolo fine sandy loam	7,500	23·8	315	6·9
Sacramento fine sandy loam	4,460	17·6	253	7·0

Strontium was determined by a General Electric model *XRD-5* X-ray spectrograph, and we are greatly indebted to Dr. L. D. Whittig for instructing us in the use of this instrument. The general procedure of Brandt and Lazar[2] was modified[3] to enable a working curve to be prepared without the use of chemically analysed samples. The soils were extracted[4] with ammonium acetate–ammonia at *p*H 9·0.

The results (Table 2) indicate five significant features. (1) Every legume species takes up more strontium than any grass—three to six times as much in many cases. (2) Within either the grasses or the legumes the variation in strontium content is not marked. (3) The amount of strontium taken up is directly related to the amount of calcium taken up. (4) There is no major discrimination between strontium and calcium by either grasses or legumes. (5) Neither the grasses nor the legumes can be ranked in the same order of strontium content for every soil, but *Bromus inermis* and *Trifolium subterraneum* are consistently highest in their respective classes. Of the legumes, *Lotus corniculatus* has the least strontium, while *Phleum pratense*, *Dactylis glomerata* and *Phalaris tuberosa* are the lowest-ranking grasses.

The results indicate that animals grazing mixed legume-grass herbage, where the legume amounts to a significant proportion of the forage, will ingest much more strontium-90 than animals grazing all-grass pastures on equally contaminated soils. It is apparent that if the strontium-90 level in milk should ever

Table 2. Strontium and Calcium Content of Pasture Species Grown on Three Different Soils

Soil / Species	Nord fine sandy loam				Yolo fine sandy loam				Sacramento fine sandy loam			
	Ca (μeq./gm.)	Sr (μeq./gm.)	Ca/Sr ratio	Sr/Ca in plant / Sr/Ca in soil extract	Ca (μeq./gm.)	Sr (μeq./gm.)	Ca/Sr ratio	Sr/Ca in plant / Sr/Ca in soil extract	Ca (μeq./gm.)	Sr (μeq./gm.)	Ca/Sr ratio	Sr/Ca in plant / Sr/Ca in soil extract
Grasses :												
Bromus inermis, Manchar	348	1·49	250	1·4	202	0·83	242	1·3	306	1·25	245	1·0
Lolium perenne, Oregon Commercial	366	1·31	279	1·1	145	0·74	195	1·6	258	0·89	289	0·9
Lolium perenne, *S*.101	390	1·19	328	1·0	165	0·71	231	1·3	249	0·89	279	0·9
Festuca elatior, Late Ötofte	352	1·19	328	1·1	136	0·65	207	1·5	240	0·89	269	0·9
Festuca arundinacea, Alta	306	1·07	286	1·1	141	0·71	197	1·5	202	0·89	226	1·1
Phleum pratense, American Commercial	235	1·01	233	1·4	112	0·59	188	1·3	131	0·59	220	1·1
Phalaris tuberosa, Harding grass	352	0·95	369	0·9	151	0·71	211	1·4	225	0·71	315	0·8
Dactylis glomerata, Potomac	235	0·93	251	1·3	141	0·65	216	1·4	198	0·77	256	1·0
Legumes :												
Trifolium subterraneum, Tallarook	1,500	4·70	319	1·0	1,050	3·99	263	1·2	1,130	4·22	268	0·9
Medicago sativa, Caliverde	995	3·81	261	1·2	680	2·44	279	1·1	812	2·65	306	0·8
Trifolium fragericum, Salinas	1,105	3·57	310	1·0	573	2·20	260	1·2	780	2·74	285	0·9
Trifolium repens, *S*.100	1,020	3·51	291	1·1	521	1·96	266	1·1	755	2·62	288	0·8
Trifolium repens, Dutch White	995	3·27	304	1·1	770	2·84	271	1·1	985	3·45	286	0·9
Trifolium pratense, Kenland	940	3·20	294	1·1	667	2·47	270	1·1	1,130	3·99	283	0·9
Trifolium repens, Ladino	976	3·09	319	1·0	770	2·74	281	1·1	1,050	3·57	294	0·9
Lotus corniculatus, Los banos	718	2·53	284	1·1	390	1·67	234	1·3	648	2·38	272	0·9

rise to a level which, maintained over a period of time, might give cause for concern, it would be desirable to restrict dairy cows to an all-grass diet. On current evidence this situation is unlikely to occur if the present level of atomic weapon testing is maintained, but in the future it might prove desirable to take this measure to reduce the strontium-90 level in milk, particularly that consumed by children. Such measures might first become necessary in regions of high rainfall, or where other local factors predispose a higher than average radiostrontium content of milk. Milk radiostrontium contents as high as 32 s.u. have been reported[5].

Where land that is relatively heavily contaminated with strontium-90 must be actively farmed, then bare fallow should be sown with an appropriate grass, no clover being included in the mixture. Established pastures should be heavily fertilized with nitrogen to encourage the growth of grass at the expense of clover.

This work was carried out in the Department of Agronomy, University of California, Davis, California.

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Plants and Fall-out

It has been suggested that the gist of certain unpublished observations on the condition of certain plants in the area of the Marshall Islands affected by fall-out from the 1954 Bikini hydrogen bomb test should be made public in order to stimulate further investigation on the subject of cumulative effects of low-level radioactivity in plants. These observations have hitherto remained unpublished because of their preliminary and inconclusive nature.

In earlier fall-out surveys of 1954 and 1955, made by non-botanical observers, in the atolls of Rongelap, Ailinginae, Rongerik and Utirik no visible effects on plants were observed, although accumulation of radioactive materials in plant tissues was demonstrated. In the 1956 re-survey, under the auspices of the U.S. Naval Radiological Defense Laboratory, only casual observations were made on the condition of the plants, attention being concentrated on collection of material for analysis. Eight coral islet stations were examined which had been affected by different intensities of fall-out.

Later study of notes made on the vegetation on these islets showed abnormal or pathological conditions in certain plant species, increasing from islet to islet in the same order as the increase in fall-out intensity. Since the observations were not made systematically, nor with the possibility of visible pathological effects in mind, only the roughest of correlations is possible. Even so, the differences were striking enough to merit further attention.

On Gegen Islet, Rongelap Atoll, the station with the greatest fall-out exposure, of a total flora of 15 species, 13 showed conspicuous pathological or abnormal symptoms, ranging from plants dead or almost so to chlorosis, dead terminal twigs and mistletoe-like abnormal growths.

On Kabelle Islet, Rongelap Atoll, next most heavily exposed, 3 species showed some damage.

On all other stations at most one or two species showed effects, but on Eniwetak Islet, Rongerik Atoll, though only two species were involved, the symptoms, defoliation and die-back of twigs, were so conspicuous as to alter the appearance of the vegetation, causing a general grey colour in place of the normal green.

On Likiep Islet, Likiep Atoll, which had scarcely any measurable fall-out, no abnormal appearances of any sort were noticed.

The plants most widely affected were: *Suriana maritima* L., which was completely dead on Kabelle Islet and partially dead on other islets where it was observed; *Cordia subcordata* Lam., which on Gegen Islet was dead or almost so, and on Eniwetak Islet, where it is the most important tree in the vegetation, had the tips of almost all its twigs dead for 10–15 cm.; and *Pisonia grandis* R. Br., which was more or less leafless on the more affected islets and bore, on Gegen Islet, curious mistletoe- or witches-broom-like leafy branches of a dark green colour which have not been noted elsewhere on this species. The defoliation of the last species is not necessarily abnormal, as it happens during severe drought periods. Its association with the stations where fall-out was relatively heavy and without other evidence of drought makes it of interest.

In all, 43 species are known from Rongelap, Rongerik and Ailinginae, the three atolls heavily affected by fall-out. Only about half these plants grow on the four islets where the heaviest fall-out was recorded. Of these, 16 species were noted to show some abnormality. Two species of universal occurrence and great abundance, *Scaevola sericea* Vahl and *Tournefortia argentea* L. f., showed no abnormal appearance whatever.

It will be noted that the total flora of these islands is very small and made up of strand species, tolerant of high salt concentration and exposure to drying winds.

I am very familiar with the flora and vegetation of coral atolls, generally, and with the Marshall Islands, especially, so that the observations are of more significance than if I had less background.

It is not suggested that these observations are positive indication of cumulative effect of fall-out. There may be other unsuspected causes. However, the correlation between intensity of observed symptoms and intensity of recorded fall-out is at least suggestive, and would seem to justify further investigation. The extreme diversity in the reactions of different species growing under the same conditions to whatever caused these effects is of great interest. It suggests the advisability of using a wide variety of plants in any set of experiments designed to investigate the effects of radioactivity, as well as those of other environmental factors. It becomes harder and harder to generalize on the influence of any factor on plants.

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Comparative Sensitivity to Radiation of Seeds from a Wild Plant grown on Uraniferous and Non-Uraniferous Soils

THE long-term effects of low-level chronic irradiation on living organisms have attracted increasing interest in connexion with the observed contamination from man-made radioactive sources over large areas of the Earth's surface. No experimental evidence exists that definite biological changes are induced in a large population under very low continuous exposure.

The assessment of sensitivity during the process of germination may provide a satisfactory approach, as seeds are available from plants of the same species that have—or have not—grown for ages in a radioactive environment, thus being continuously irradiated. We used seeds of *Andropogon filifolius* (Nees) Steud, a perennial grass[1], collected by one of us on neighbouring uraniferous (Kasompi) and non-uraniferous, but otherwise similarly mineralized, soils (Dikuluwe) in Katanga (Belgian Congo). The dose received by the sexual or somatic cells of these plants is impossible to calculate, mainly because the radioactivity of the superficial layers of the soil is extremely variable—from 10 to 50 times background.

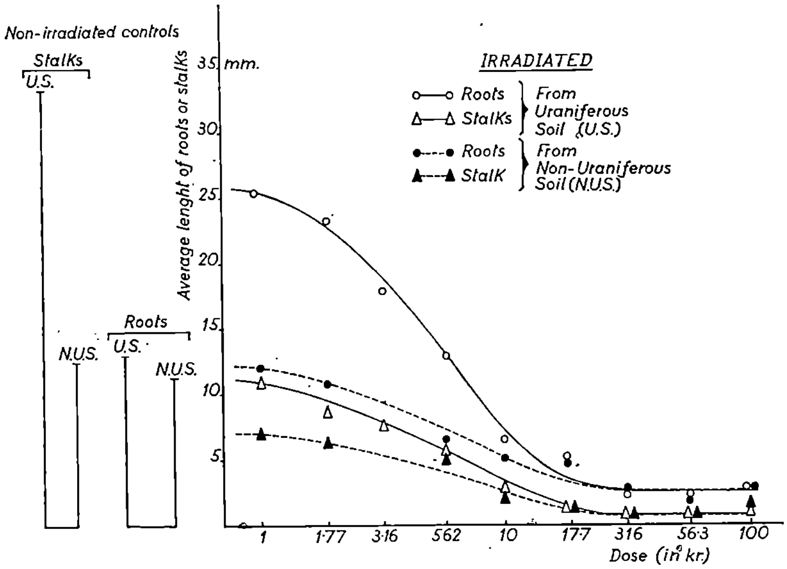

Fig. 1

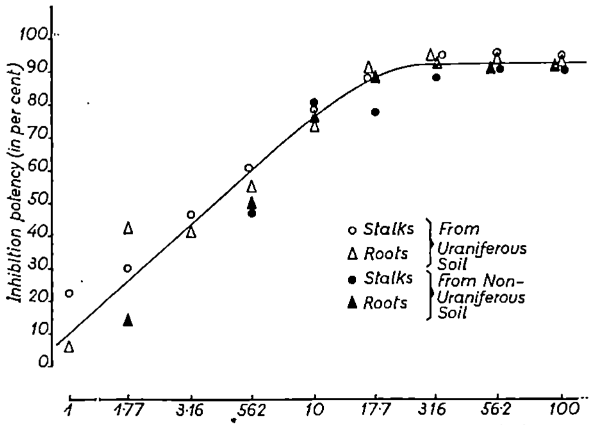

Fig. 2

Table 1

Dose (r)	Germination (per cent)	
	Uraniferous soil	Non-uraniferous soil
0	30·0	18·0
1,000	26·7	18·0
1,770	24·0	22·0
3,160	30·7	22·0
5,620	28·0	24·0
10,000	24·6	11·5
17,700	24·7	14·0
81,600	21·9	13·3
56,200	19·3	11·1
100,000	19·9	17·3

Groups of seeds (150) soaked for 12 hr. from both soils were irradiated simultaneously on moist filter paper at different doses with a Siemens 'Stabilivolt' (200 kV.; 20 m.amp.; no filter; source-target distance: 30 cm.; rate, 700 r./min.). All seeds were grown in a greenhouse on moist filter paper. Three criteria were investigated: germination, and maximal lengths of stalks and roots[2] at the time of death of the plantlets. The percentage of 'normal' germination and length of stalk and roots were estimated from un-irradiated control groups (± 1·800 seeds). The results are shown in Table 1 and Fig. 1.

Seeds originating from uraniferous soil exhibit a higher percentage of germination, and plantlets develop stalks and roots of greater average length. Germination is not significantly inhibited by radiation in the range used. At any dose-level, the average length of roots and stalk is greater in plants from uraniferous soil. The potency of radiation in inhibiting growth of roots and stalks may be expressed as the percentage of shortening of initial length per roentgen. It decreased exponentially with dose and reached a plateau at the 20,000 *r.* dose-level; no significant difference was evident between either series (Fig. 2). However, the observed differences between percentages of germination and lengths of organs of plants from uraniferous soils and those from non-uraniferous soils lead to the conclusion that the two populations are different. The chronically irradiated population possesses higher vitality. Whether selection or adaptation or both are responsible is an open matter. In any event, enhancement of biological potentialities rather than degeneration has apparently resulted from long-continued low-level irradiation of *Andropogon filifolius.* This experiment is now being repeated with another species of *Andropogon.*

We thank the officers of the Union Minière du Haut Katanga and especially the geologists for their kind collaboration in collecting specimens.

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Modification of the Oxygen Effect when Bacteria are given Large Pulses of Radiation

Many biological materials, including bacteria, have been shown to be more readily damaged when oxygen is available to the cell at the time of irradiation than when it is absent[1,2]. *Serratia marcescens* shows this enhanced sensitivity to radiation—the so-called 'oxygen effect'—almost to the full extent when a suspension of them is saturated with a gas mixture containing only 1 per cent oxygen and 99 per cent nitrogen, provided the radiation is given at normal dose-rates of about 1,000 rads/min. Typical inactivation curves for this organism using 1·5 MV. X-radiation from a pulsed linear accelerator are given in Fig. 1. Using the intense electron beam from the same linear accelerator, however, a dose of some 10–20 kilorads can be delivered in 2 microsec. The results quoted below indicate that when such large single pulses are used, the same bacteria saturated with the same oxygen–nitrogen mixture show the lower sensitivity corresponding to anaerobic irradiation. This is thought to be due to the fact that the first few kilorads of the electron pulse remove dissolved oxygen from the interior of the bacterium by radiation-induced reactions. During the remainder of the pulse the bacterium will thus be receiving radiation under essentially anaerobic conditions. Even though dissolved molecular oxygen may not be entirely removed by the radiation from the extracellular liquid, this cannot penetrate the cell by diffusion in the 2 microsec. that the pulse lasts.

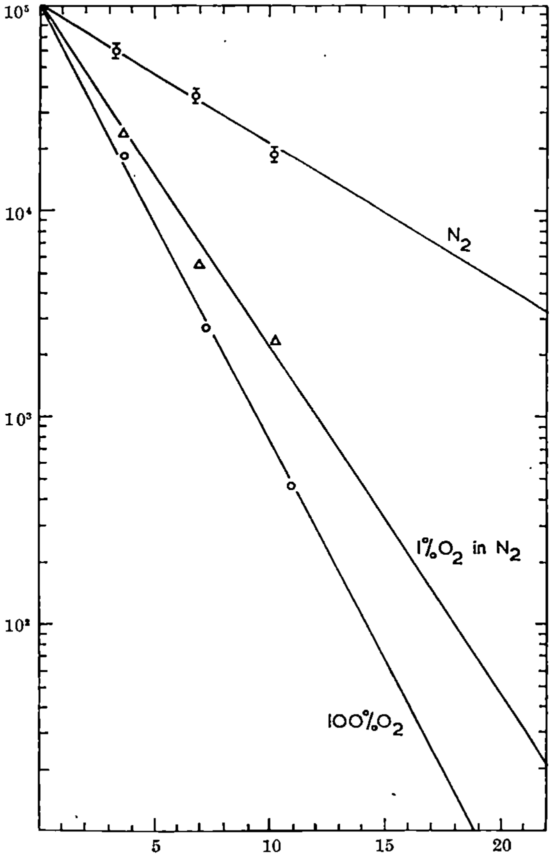

Fig. 1. Number of *Serratia marcescens* surviving from 10^5 bacteria after 1·5 MV. X-radiation while equilibrated with nitrogen, oxygen and a mixture of 1 per cent in nitrogen. Dose-rate = 600 rads/min.

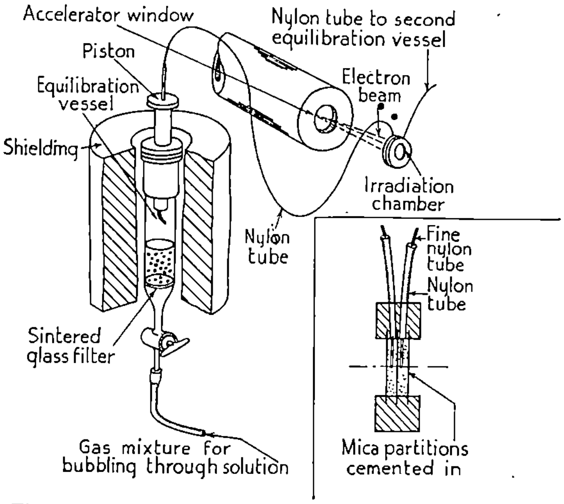

Fig. 2. Apparatus for equilibrating the bacterial suspensions and filling the irradiation chamber. Inset, an enlarged view of the irradiation chamber showing the two compartments

The experimental apparatus is shown in Fig. 2. In order to obtain an adequate dose, the irradiation chamber had to be placed about 10 cm. from the exit window of the accelerator, and to obtain a tolerably uniform dose distribution its size had to be restricted to 0·2 ml. The irradiation chamber had two compartments, one behind the other, separated only by a thin mica foil so that every electron pulse passed through both. One was generally filled with a suspension of bacteria saturated with nitrogen and the other with a suspension of bacteria saturated with the gas mixture under test.

The chambers were too small to permit internal gas bubbling, and each bacterial suspension was therefore equilibrated with the gas under test in a separate glass funnel closed by an air-tight plunger. Gas escaped from this through a fine nylon tube which terminated inside the irradiation chamber. After an adequate period of equilibration, the bacterial suspension was transferred to the irradiation chamber by depressing the plunger until the nylon tube dipped below the surface of the liquid, and the suspension was forced along into the cell. Irradiation was completed within a minute of transferring the bacteria, and during this time the removal of oxygen by respiration was found to be negligible at the bacterial titre used. Control samples were taken from both equilibration vessels immediately after each pulse of electrons. The equilibration vessels were heavily shielded during irradiation.

In a preliminary control experiment, when both compartments were filled with bacteria saturated with oxygen-free nitrogen, the ratio of the doses received in the separate compartments could be measured biologically by the survival of the bacteria, as indicated by visible colony counts on nutrient agar plates. The same ratio could be measured physically by the ultra-violet absorption induced in small 'Perspex' monitors[3] placed in the position of the cell compartments. The two estimates of the dose ratio were:

$$\frac{\text{Dose in back compartment}}{\text{Dose in front compartment}} = 1{\cdot}36 \text{ by bacterial survival}$$

$$= 1{\cdot}22 \text{ by ultra-violet absorption in 'Perspex'}$$

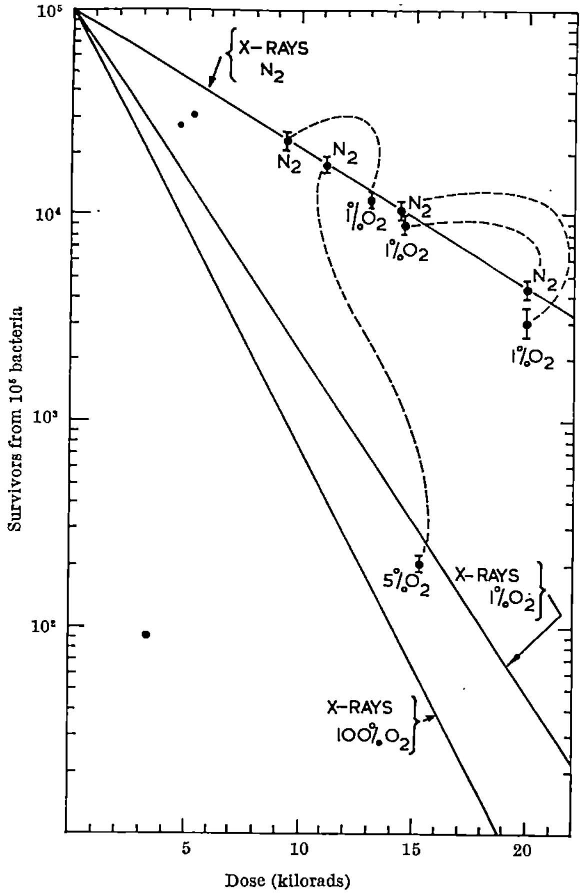

Fig. 3. The effect of single electron pulses on *Serratia marcescens*. The straight lines are X-ray survival curves taken from Fig. 1. The pairs of points joined by dotted lines are the survivors from the two compartments of the double cell, after a single pulse of electrons

The final conclusions were made largely independent of any differences in dose delivered to the two cells by doing each experiment twice—once with the reference suspension of nitrogenated bacteria in the front compartment and once with it in the back compartment. In plotting the results the biological estimate of the ratio, that is, 1·36, has been used as this was considered the more direct measurement; but the conclusions would be quite unaffected if the other value 1·22 had been used.

Fig. 3 is a plot of the observations made with pulsed doses in relation to the straight lines for lower dose-rates taken from Fig. 1. For each radiation the survival in the anaerobic compartment has been taken as a measure of the dose and is therefore plotted on the nitrogen line. The point derived from the other compartment is linked with the corresponding nitrogen point by a dotted line. Bacteria which had been equilibrated with 1 per cent oxygen in nitrogen showed approximately the anaerobic sensitivity, whereas bacteria equilibrated with 5 per cent oxygen in nitrogen showed nearly the full oxygen effect. In the latter case, there was evidently too much dissolved oxygen within the bacillus for it to be removed by the early part of the electron pulse and so most, or perhaps all, of the dose was delivered in the presence of sufficient dissolved oxygen.

An alternative explanation of the effects described above, based on radiation-chemical interaction between clusters of ions formed in adjacent electron-tracks in the single pulse, is unlikely to be correct. In order to approach the concentration of ions found in the core of an α-particle track an instantaneous dose of some 10^9 rads would be required.

Experiments with the pulsed irradiation are continuing to determine more exactly the shape of the survival curves for different initial concentrations of dissolved oxygen.

We are greatly indebted to Dr. L. H. Gray, who suggested this experiment, and has throughout given his advice and encouragement.

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Action of Ultra-violet Light on Skin: Effect of the Histamine Liberator 48/80 and Methotrimeprazine

Rottier and Mullink[1] irradiated human skin with ultra-violet light at a place where the horny layer had been removed by repeatedly applying adhesive tape. The erythemal reaction practically disappeared at wave-lengths 250–260 mμ, but increased at 300 mμ. They therefore suggested that photolysable substances from the stratum corneum were responsible for the erythemal reaction caused by ultra-violet light of wave-length 250–260 mμ. The problem concerning the mediator substance in ultra-violet erythema still seems to be unsolved. Lewis and Zotterman's[2] suggestion that it should be histamine has not been confirmed[3]. Recently, much interest has been focused on 5-hydroxytryptamine as a possible mediator in the production of œdema.

It is therefore of interest to obtain information about the role taken by histamine and 5-hydroxytryptamine in the production of ultra-violet light erythema at the two wave-lengths mentioned above, both in intact skin and in skin where the superficial layer has been removed by tape. This has been done by treating the animals subjected to irradiation with 48/80, which liberates both histamine and 5-hydroxytryptamine, and with methotrimeprazine (7044 *RP*), an inhibitor of 5-hydroxytryptamine[4].

Experiments were performed on albino male rats (100–120 gm.) where the stratum corneum had been removed from one side of the shaved back by applying adhesive tape. For irradiation, the rats were fastened to boards and covered with black rubber sheets with three 16-mm. holes on each side of the spine. Radiation of wave-length 280–330 mμ was obtained from a water-cooled, high-pressure mercury arc (Philips *SP* 500 W.) provided with filter (2 mm. Jena *WG* 7 + 10 mm. $NiSO_4.6H_2O$, 600 gm./l.). For the wave-length 253·7 mμ, a low-pressure mercury arc was used. The doses, measured by chemical actinometry[5], varied from about 2×10^{16} to 5×10^{18} $h\nu$/cm.². The degree of tissue damage was estimated from the leakage of intravenously injected Evans blue into the irradiated areas[5,6].

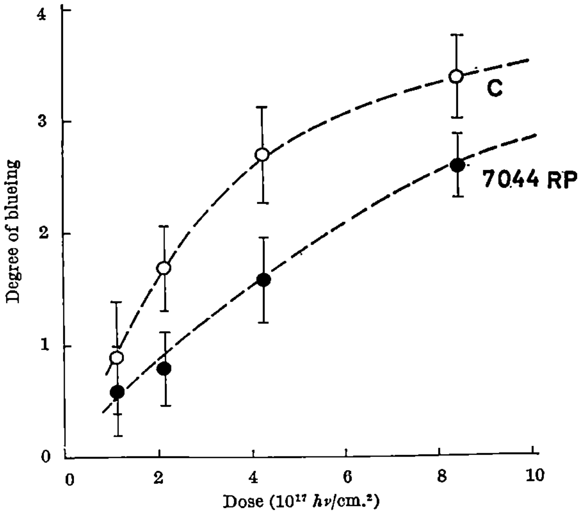

Fig. 1. Degree of blueing (tissue injury) versus dose for rats treated with 7044 *RP* after irradiation (●) and for control animals (○). The vertical lines indicate the standard deviation from the mean

Of the 60 animals used, one third were pretreated intraperitoneally with compound 48/80 in increasing doses from 100 to 700γ for 7 days previous to irradiation. Another third were injected intravenously immediately after irradiation with 0·5 mgm. 7044 *RP*. The remainder were used as controls, and irradiated simultaneously with the other animals.

In all cases, and for both wave-lengths, removal of the corneum caused increased erythemal reactions at both 253·7 and 280–330 mμ. Thus for rats, the results at the wave-length 253·7 mμ are not in accordance with those found by Rottier and Mullink[1] for humans. To exclude the possibility that the difference is due to the different species used, experiments were also performed on rabbits and humans; in both cases removal of the corneum caused an increased reaction at the wave-length 253·7 mμ.

No observable change in the degree of blueing could be observed by depleting the rat-skin of its content of histamine and 5-hydroxytryptamine by use of compound 48/80.

On the other hand, the interesting observation was made that the ultra-violet light reaction in rats at 280–330 mμ could be decreased by injection of a 5-hydroxytryptamine inhibitor immediately after irradiation. This is evident from Fig. 1. These results, together with the observation[3] that a histamine inhibitor has no effect, indicate that the mediator substance in the ultra-violet reaction is not histamine, but it may be 5-hydroxytryptamine.

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CYTOLOGY and GENETICS

Colour-blindness in Klinefelter's Syndrome

Males with testicular hypoplasia (Klinefelter's syndrome) are of two cytological types. A minority has sex-chromatin-negative nuclei as have normal males, whereas the majority has sex-chromatin-positive nuclei as have normal females. The demonstration of the male-determining property of the mammalian *Y*-chromosome, proved for man[1] and mouse[2], had led to a clarification of the chromosomal status of sex-chromatin-positive Klinefelter individuals. They are *XXY*[1,2].

It is well known that the frequency of females homozygous for recessive genes which are located in the *X*-chromosome is much lower than of hemizygous affected males. Thus, *X*-linked red-green colour-blindness occurs among males of European ancestry in the order of 8 per cent, whereas in females it is only about 0·5 per cent. It has been thought that a genetic correlate of the presence of two *X*-chromosomes in sex-chromatin-positive Klinefelter individuals would be a very low frequency of colour-blindness, equivalent to that in females. This expectation seemed to be borne out by studies of Polani, Bishop, Lennox, Ferguson-Smith, Stewart and Prader[3]. They tested 55 sex-chromatin-positive Klinefelter patients for their colour vision and found that none was affected. Additional tests have brought the total number to 72, all with normal colour vision (Polani, R. E., personal communication). Different results, however, were reported by Nowakowski, Lenz and Parada[4]. Among 34 sex-chromatin-positive Klinefelter individuals they detected three affected persons, two of whom were deuteranomalous and one protanopic. It will be shown that the findings of the two groups of investigators are compatible with each other and that they may provide new insight into the behaviour and constitution of human chromosomes.

One of the deuteranomalous men had a deuteranomalous mother and a father with normal colour vision. Assuming *XXY* constitution of the propositus, he would be expected to be deuteranomalous if he originated from a non-disjunctional egg carrying two maternal *X*-chromosomes fertilized by a sperm carrying a *Y*-chromosome. The other deuteranomalous and the protanopic propositus both had normal fathers, and mothers who, on independent evidence, were heterozygous for an allele for defective colour vision. How can the defective colour vision of the presumably *XXY* propositi be explained? There is a possibility, of unknown strength, that they are manifesting heterozygotes[5]. But in *Drosophila* and other organisms the phenomenon of homozygous recessive offspring from heterozygous mothers mated to hemi- or homo-zygous dominant males is well known. It occurs in consequence of crossing-over and non-disjunction. If the chromosomes of the mother carry the alleles *A* and *a*, then at meiosis four chromatids, two carrying *A* and two *a*, will be present. If no crossing-over occurs between the kinetochore and the locus of *A*, non-disjunction at the first meiotic division will produce an *Aa* egg; but if within the region designated, certain types of cross-overs occur, an 'equational' non-disjunctional egg of the type *AA* or *aa* can be formed. This apparently had occurred in the eggs which gave rise to the two presumably homozygous Klinefelter individuals with defective colour vision from heterozygous mothers.

The frequency of homozygosis due to crossing-over and non-disjunction is a function of the distance between the kinetochore and the locus concerned. With a map distance between these two so great as to result in free recombination, the maximum of 16·7 per cent of recessive homozygosis is obtained (leaving out minor complications). In other words, as the result of non-disjunction of the *X*-chromosomes in heterozygous females a maximum of about one-sixth of the *XXY* sons could be homozygous recessives. Since the frequency of women heterozygous for one or the other of the alleles for *X*-linked colour-blindness is about 15 per cent, maximally one-sixth of their Klinefelter sons from non-disjunction in the mothers, or maximally 2·5 per cent of all Klinefelters of this origin, could be colour-blind. In addition, approximately 0·5 per cent of Klinefelters would be colour-blind coming from homozygous affected mothers. A further source of colour-blind Klinefelter sons could be non-disjunction of the *X*- and *Y*-chromosomes in colour-blind men married to heterozygous or homozygous affected women. Approximately 0·5 per cent of Klinefelter individuals would be colour-blind due to this mechanism.

Depending on the relative proportion of individuals who owe their Klinefelter status to non-disjunction in the mother as compared to the father, the frequency of colour-blindness among them would vary between a maximum of 2·5 + 0·5 = 3 per cent and 0·5 per cent. The maximum expectation is statistically compatible with the observations of both groups of investigators, namely, 0 affected to 72 not affected, and 3 affected to 31 not affected. Combining the data results in 3 affected out of 106 individuals, or 2·8 per cent. The statistical uncertainty of this value is, of course, great.

An alternative hypothesis to the one proposed here would be that in man equational exceptions originate without crossing-over as the result of non-disjunction at the second meiotic division. If this were the only source of colour-blind Klinefelter males, they would constitute 7·5 per cent (from heterozygous mothers) plus 0·5 per cent (from homozygous mothers) of all propositi.

All three colour-blind individuals originated after non-disjunction in their mothers. Their frequency of 2·8 per cent suggests that most Klinefelter males with positive sex chromatin come from this source. Assuming that the first hypothesis proposed is correct, it suggests that the frequency of crossing-over among non-disjunctional eggs, leading to equational exceptions, is high. Furthermore, the high frequency of equational exceptions suggests that the locus for colour-blindness lies at a considerable distance from the kinetochore of the *X*-chromosome.

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Two Types of Ribonucleoprotein in the Nucleolus of Mammalian Cells

NUCLEOLAR differentiation has been recognized since the time of Gustav Valentin. Agassiz[1] referred to a body within the nucleolus of the turtle egg as the "Valentinian vesicle". Montgomery[2] and Heidenhain[3] called this structure the nucleolinus. Recently, it has been suggested that the appearance of vesicular or solid nucleolini is due to the presence of a reticulum or thread called the nucleolonema[4]. None of the procedures that reveal nucleolonemata[4-6] has any cytochemical significance. Serra[7] suggested that the intranucleolar differentiation revealed by empirical procedures may be the result of physical rather than chemical inhomogeneity within the nucleolus. Chemical differences have, however, been found in the nucleoli of plant cells. Chayen *et al.*[8] demonstrated one or more inner zones of protein material and an outer zone that probably contained ribonucleoprotein. Further evidence of cytochemical differentiation in the nucleolus has been provided by a new stain for nucleoproteins[9].

Normal mouse and rat liver and pancreas, rat sympathetic ganglion, the Ehrlich and Krebs 2 ascites tumours, sarcoma 180 and a human epidermoid carcinoma were prepared by the toluidine blue–molybdate method to produce stage 1 of staining[9]. By this means, ribonucleoprotein of the parachromatin (nuclear sap) was coloured purple and that of the greater part of the nucleolus was stained green[9]. The nucleoli of many neurones, the parenchymal cells of liver and pancreas and neoplastic cells also contained minute unstained vacuoles and a variable amount of metachromatic ribonucleoprotein. The latter was most prominent in transplantable tumours, and especially in the Ehrlich tumour, where it was present in the nucleoli of every interphase cell in the form of minute granules, larger hollow spheres or clusters of hollow spheres (Fig. 1). Under the phase microscope numerous vacuoles were observed in the nucleoli of living cells (Fig. 2). Comparison of the nucleolus in the living cell with that in the stained preparations revealed that the metachromatic ribonucleoprotein was present in or around some, but not all, of the vacuoles (Figs. 1 and 2). This

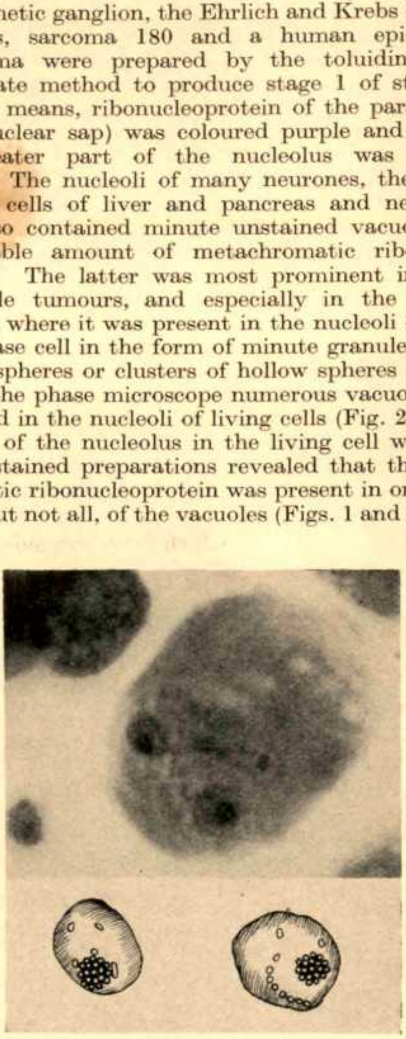

Fig. 1. Ehrlich ascites tumour cell stained by the toluidine blue–molybdate method (stage 1). Several minute vacuoles are visible in the green-staining outer zones of two prominent nucleoli. A cluster of metachromatic vesicles gives the appearance of a slightly eccentric internal body. (×1,400)

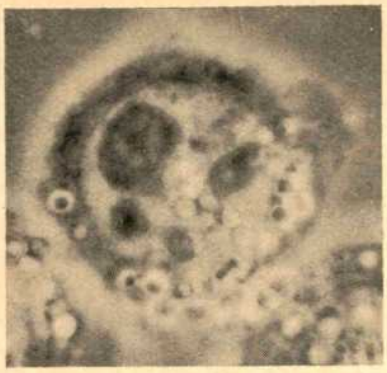

Fig. 2. Phase microscope photograph of an Ehrlich ascites tumour cell. A ring of vacuoles surrounds a dark structure in the nucleolus, in the centre of which a lighter vacuole is present. The central structure stains metachromatically by the toluidine blue–molybdate method. (× 1,400)

nucleolar ribonucleoprotein was coloured in exactly the same way as the nuclear parachromatin in all stages of staining by the toluidine blue–molybdate method and did not stain after pretreatment with ribonuclease or hot trichloracetic acid[7]; it may therefore be called the nucleolar parachromatin. In the Ehrlich ascites tumour the nucleolus often persisted throughout mitosis but was not incorporated into the daughter nucleus. In early prophase the nucleolar parachromatin was frequently at the rim of the nucleolus; during later prophase it was no longer detectable, whereas the vacuolated green-staining nucleolus was clearly visible in metaphase, anaphase and telophase. The nucleolar parachromatin was probably extruded from the nucleolus during prophase to contribute to the accumulation of granular parachromatin that took place at this time[9]. In the daughter nucleus the earliest sign of re-formation of the nucleolus was a metachromatic body which later acquired an outer coating of amorphous or vacuolated green-staining ribonucleoprotein.

The exact relationship of the two types of ribonucleoprotein in the nucleolus to the nucleolonemata and the nucleolini is not clear. In electron micrographs the nucleolonema was virtually absent in the Ehrlich tumour[6], in which the nucleolar parachromatin was most prominent. The absence of thread-like structures in the Ehrlich tumour was confirmed in electron micrographs kindly prepared by Mrs. Darlene Brindley in this laboratory. Similarly, the nucleolar parachromatin was least prominent in liver cells, where, according to Bernhard *et al.*[6], the nucleolus consists almost entirely of filaments. Although darker zones, resembling the nucleolar parachromatin, could be demonstrated around nucleolar vacuoles in rat sympathetic ganglion cells by Sotelo's method[4], the same technique did not reveal any internal structure, other than vacuoles, in the nucleoli of the Ehrlich tumour. The site and amount of nucleolar parachromatin is therefore unrelated to the ability of nucleoli to reduce iron or silver salts[4] or osmium tetroxide[5,6] to produce thread-like formations or nucleolonemata. Solid and hollow structures, resembling the nucleolini of the classical cytologists, were, however, demonstrable in Ehrlich cells stained with iron hæmatoxylin. Thus, the physico-chemical differences in ribonucleoprotein that determine differential staining by the toluidine blue–molybdate technique may also be responsible for differences in affinity for hæmatoxylin.

We wish to thank Mr. Roscoe H. Liles for valuable technical assistance and Mr. Walter C. Ashe for the drawing.

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Size Relationship of Oocytes and their Nuclei in Two Species of Ascidians

NUCLEAR intervention in cytoplasmic growth and differentiation has formed the subject of many studies during recent years. One significant result from these studies is the recognition of the major part played by the nucleolus in the developing egg[1-3]. A recent review by Vincent[4] has surveyed the problem.

The determination of size of the nucleus and nucleolus in different stages of growth of the oocyte is important in such a study. Very little work on volume relationships of the different cell structures during growth has been done, and, so far as I am aware, no information is available regarding ascidian oocytes. This communication presents the size relationships of the cell nucleus and nucleolus in two species of ascidians belonging to two different families, namely, *Ecteinascidia thurstoni* Herdman (Fam. Perophoridae : Enterogonia) and *Pyura* sp. (Fam. Pyuridae : Pleurogonia). *Ecteinascidia* is a viviparous form and *Pyura* is oviparous.

Fig. 1 presents the relationships of the diameter of the nucleolus, nucleus and the oocyte. In *Pyura* the oocyte grows to 150μ, while in *Ecteinascidia* it reaches 300μ in diameter. In both species, the diameter of the nucleus increases with increase in diameter of the oocyte. However, the increase in *E. thurstoni* is more striking than that in *Pyura*. In regard to the nucleolus in both species, there is an initial increase in size, which reaches the maximum —10μ diam.—when the oocyte has attained the diameter of 60μ in *Pyura* and 70μ in *Ecteinascidia*. There is no further increase in size of nucleolus after this and the curve levels off. The size relationships shown here for ascidian oocytes resemble those described for amphibian[5] and starfish[4] oocytes.

From these observations it would appear that, so far as can be judged by size, the nucleolus appears to be active only in the early stages of growth of the oocyte and not in the later stages. If the nucleolus plays any part at all in the synthesis of cytoplasmic proteins[1,2] it is clear that this activity is restricted to the early growth of the oocyte. Later contributions must come from some other source. Berrill[6] has posed the problem of the role of the follicle and 'test'

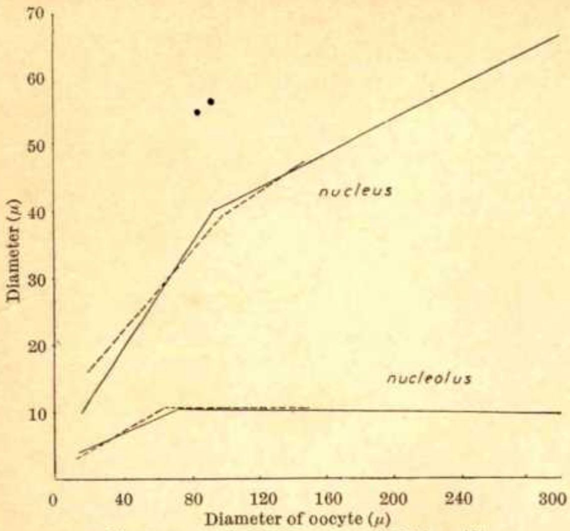

Fig. 1. ----, *Pyura*; ———, *Ecteinascidia*

cells in the growth of the ascidian oocyte. My observations on the later history of oocyte growth in both *Ecteinascidia* and *Pyura* lead me to believe that the activity of the nucleolus ceases, the follicle cells and 'test' cells take over, and, by their contributions, assist in the cytoplasmic synthesis. In these later stages, the outer half of the oocyte is filled with periodic acid–Schiff-positive substances, granules in *Ecteinascidia* and plaques in *Pyura*, and there is reason for believing that they come from the follicle and 'test' cells surrounding the oocyte. The periodic acid–Schiff reaction is indicative of the presence of protein carbohydrate complexes and it is highly probable that these are the predominant products of later synthesis.

A detailed study of the origin and nature of these substances is in progress and will be reported elsewhere.

I am indebted to Prof. B. R. Seshachar for his guidance and criticisms. Thanks are due to the National Institute of Sciences of India for awarding me a junior fellowship.

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Effect of Colchicine on the Utilization of Thymidine labelled with Tritium during Chromosomal Reproduction

EXPERIMENTS[1] designed to verify the findings of Taylor, Woods and Hughes[2] on the incorporation of thymidine labelled with tritium in the deoxyribonucleic acid in chromosomes of growing root meristems of seedlings of *Vicia faba* have produced evidence that colchicine influences either the synthesis of the acid or its subsequent distribution among sister chromatids at metaphase. This evidence was derived from two types of experiment.

In the first, colchicine was not used and chromosomes with the sister chromatids both labelled were regularly found in metaphases and anaphases at 24 hr. after labelling and frequently also at 48 hr., that is, after approximately two cell cycles. Since after 48 hr. about 12 per cent of the metaphases contained some chromosomes labelled in both chromatids and others only in one, it was not of overriding importance to determine whether such nuclei were undergoing their first or second mitosis after the labelled thymidine was applied, though the indications were in favour of regarding them as second divisions.

In the second experiment, colchicine was used in the following way. Seedlings were grown in tap-water containing 0·05 per cent colchicine to which labelled thymidine was added 1 hr. later. This was replaced after 8 hr. by fresh tap-water with 0·05 per cent colchicine, and roots were fixed after 20 and 24 hr. In both samples autoradiographs showed some chromosomes labelled in only one chromatid already in the first mitosis after labelling. Closely similar results have since been obtained with concentrations of colchicine ranging from 0·025 to 0·1 per cent, treatment commencing 2 and 4 hr. before the application of labelled thymidine (Fig. 1).

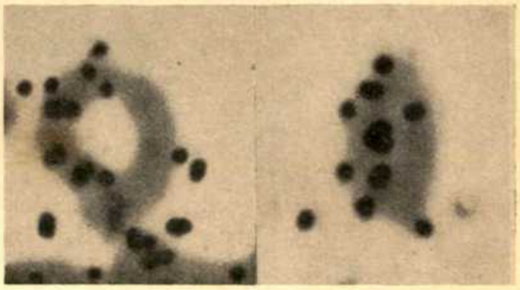

Fig. 1. Autoradiographs over *Vicia* chromosomes from *C*-metaphases at the first mitosis after labelling with ^{3}H-thymidine, showing labelling in one chromatid only. Left, from a root of a seedling grown for 2 hr. in 0·025 per cent colchicine in tap-water prior to treatment for 7 hr. with 0·025 per cent colchicine and ^{3}H-thymidine, followed by 0·025 per cent colchicine in tap-water for 13 hr. Right, after 4 hr. in 0·025 per cent colchicine; 0·025 per cent colchicine and ^{3}H-thymidine 7 hr.; 0·025 per cent colchicine 9 hr. Squash preparations stained in toluidine blue after autoradiography. (× 2,700)

These results seemed to contradict the findings of Taylor *et al.*, who reported that in their experiments all chromosomes were labelled in both chromatids at the first mitosis, while all were labelled in only one chromatid at the second mitosis. In a more recent publication, however, Taylor[3] reports two instances of chromosomes labelled in both chromatids in roots of *Bellevalia romano* in *C*-metaphases in the second division. The frequency of such chromosomes seems to be much lower than in our experiments on *V. faba* without colchicine. C. H. Ockey (personal communication), in agreement with our findings, has found chromosomes with sister chromatid labelling together with chromosomes labelled only in one chromatid in *V. faba* roots not treated with colchicine and fixed 40 hr. after labelling.

Woods and Schairer[4] grew seedlings of *V. faba* in nutrient solution containing labelled thymidine and 0·03 per cent colchicine for 12 hr. and compared them with plants grown in nutrient solution plus labelled thymidine for 8 hr. followed by nutrient solution with colchicine without labelled thymidine for 6 hr. Their experiment thus differs from our colchicine experiment in two important aspects: they omitted pretreatment for 1 hr. with colchicine

Table 1. RE-DISTRIBUTION OF NEWLY SYNTHESIZED DEOXYRIBONUCLEIC ACID
(Based on the experimental data of Woods and Schairer. 2 × 25 chromosomes each treatment)

Suggested ratio	1 : 1		1·5 : 1		1·75 : 1	
Treatment	χ^2	P	χ^2	P	χ^2	P
Control	43·61	0·72	23·44	>0·99	55·07	0·3
Colchicine	35·29	0·94	19·1	>0·99	45·91	0·5

The values for χ^2 for the ratios 1·5 : 1 and 1·75 : 1 were calculated on the assumption that the chromatid showing the higher number of grains represented the more heavily labelled one; the inverse probability of the more heavily labelled chromatid showing fewer grains was neglected. It is considered unlikely that the error thereby introduced should affect the conclusions.

to ensure that this agent was already active when labelled thymidine was added and the concentration of colchicine was lower than in our experiments. It should also be noted that the controls were kept in colchicine for 6 hr. after labelling and that the concentration of labelled thymidine was also different from ours. The extent to which these factors influence experimental results is under investigation.

Woods and Schairer counted grains in autoradiographs over 25 metaphase chromosomes in each sample and found by the chi-square test that their results were compatible with equal re-distribution of newly synthesized deoxyribonucleic acid among the sister chromatids at metaphase. We have examined the statistical significance of their results (Table 1). Since the chi-square tests obviously do not exclude the possibility of the re-distribution of newly formed deoxyribonucleic acid being in any ratio between 1 : 1 and 1·75 : 1 it has to be concluded that their results are not sufficiently accurate either to detect a change due to colchicine in this ratio within the limits stated or to contradict previous results by Plaut and Mazia[5], even if experiments on *V. faba* could be regarded as conclusive for *Crepis*. It is of interest to note that Plaut and Mazia calculated 2–3 sub-units per chromosome, which seems to agree well with the fit obtained for a factor of 1·5 : 1 in Table 1.

Woods and Schairer suggest that our observation of chromosomes with singly labelled chromatids at the first mitosis in roots of *V. faba* treated with colchicine is due to neglect of the influence on observations of absorption of β-particles in chromatids separated from the film by a layer of cytoplasm or other organic matter. The much-discussed short range of β-particles emitted by tritium was known to us when the autoradiographs were analysed and all chromosomes showing singly labelled chromatids were checked and doubtful ones rejected. Ockey (personal communication) and ourselves have found that the autoradiograph due to one labelled chromatid is still continuous where it is crossed by an overlying unlabelled chromatid. Although such differences in level can easily be seen by focusing, such chromosomes would certainly have been rejected by us. For these reasons, which inevitably introduce a certain element of subjectivity, and because of the foreseeable low accuracy, no grain counts were undertaken. It should be stressed that we never suggested that colchicine might affect the distribution of new deoxyribonucleic acid in all chromosomes; the claim was that chromosomes labelled in only one chromatid were found in significant numbers in metaphases at the first mitosis under the conditions of our experiment. In this sense the results of Woods and Schairer merely show that among the 50 chromosomes (that is, the complement of slightly more than four complete nuclei) which they accepted for grain counts no chromosome labelled in only one chromatid was found.

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BIOLOGY

Observations by Electron Microscopy on the Structure of an Acephaline Gregarine (*Apolocystis elongata*, Phillips and MacKinnon)

Apolocystis elongata lies in the seminal vesicles of the worm *Eisenia foetida* (Sav.). As we have seen by light microscopy, *Apolocystis* possesses a cuticle thickly covered by a pile of short hair-like processes each about 4μ long and 0·5μ thick. The processes do not show obvious signs of movement. The animal is a passive feeder. In our investigation by electron microscopy we have been particularly interested in determining the ultra-structural organization of the body-wall and hair-like processes.

Trophozoites of *Apolocystis* were fixed in 1 per cent osmium tetroxide solution buffered to *p*H 7·3[1], and embedded in a 3 : 1 mixture of *n*-butyl and *n*-methyl methacrylate. Ultra-thin sections were cut with a glass knife, mounted on to copper grids previously covered with a carbon film and examined with a Siemen's Elmiskop 1*a*.

The surface of the gregarine is covered with a thin, highly osmiophilic layer about 100 A. thick which covers a sheet-like array of vesicles, about one vesicle in depth. Each vesicle is about 200–300 A. in diameter and its limiting membrane is about 50 A. thick. The vesicles lie close to each other, so that in cross-section the body-wall appears to be delimited by a double membrane, the outer one corresponding to the membrane first described above and the inner one to the limiting membranes of the vesicles. Tangential sections through the body-wall show that the vesicles are arranged alternately. The general impression gained from such sections is that the body-wall is honeycombed with minute pores although, at present, we have no evidence that they are true pores in the sense that they open to the exterior and place the interior of the body in direct communication with the environment.

The electron microscope has revealed that the hair-like processes seen by light microscopy are simply finger-like evaginations of the body-wall (Fig. 1). The surface of each process has the same ultra-structural organization as the body-wall. Tangential sections through the surfaces of the 'hairs' reveal the honeycomb arrangement of the vesicles described above most clearly (Fig. 2). The interstices of the vesicles are filled with a weakly osmiophilic substance. Oblique sections through the long axis of the 'hairs' show what appear to be elongate fibres with cross-banding. Careful examination at high

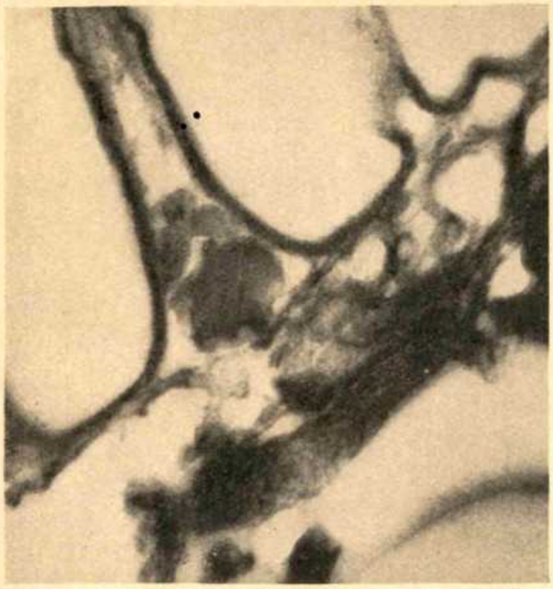

Fig. 1. Micrograph showing that the 'hairs' seen by light microscopy are finger-like evaginations of the body wall. At the base of one of the 'hairs' is a dense body of irregular outline and three smaller inclusions. Beneath the body wall is a membranous reticulum which in one region is concentrated to form an elongate body. (× 40,000)

resolution, however, shows that such 'fibres' are simply chains of vesicles, that is, the plane of section had passed through part of the wall. This interpretation is confirmed by the absence of fibres or any other osmiophilic content when the hair-like processes are seen in cross-section. In some micrographs we have observed a very dense osmiophilic granule of irregular outline and two or three smaller, and less-dense, spheroidal inclusions lying at the base of a 'hair' and projecting into it.

Functionally the hair-like processes seem to be a means of increasing the body-surface of the animal, thereby facilitating intake of nutriment and oxygen and elimination of waste products. The vesicles which lie in the body-wall probably serve essentially the same function.

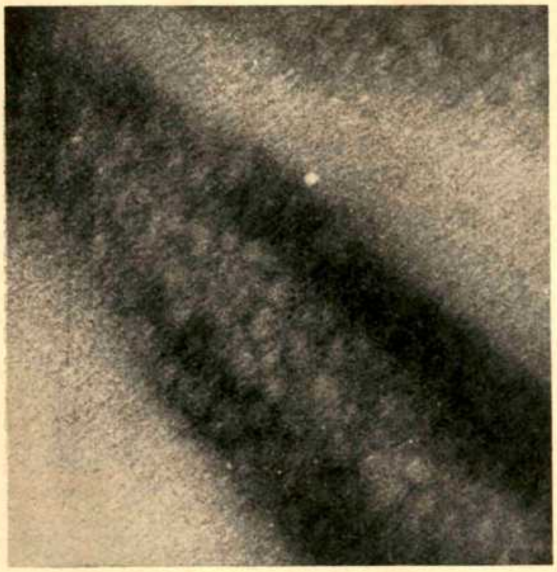

Fig. 2. Tangential section through the wall of a 'hair' to show the honeycomb arrangement of the small vesicles described in the text. (× 160,000)

Beneath the body-wall, underlying the vesicular system, is a complex network of membranes embedded in a homogeneous slightly osmiophilic substance (Fig. 1). The membranes and accompanying substance are generally separated from the vesicles by a clear (non-osmiophilic) zone of variable depth of the order of about 1μ. Each membrane is about 100 A. thick. Compared with inclusions seen in metazoan cells the network of membranes most closely resembles the endoplasmic recticulum[2]. Examination of light microscopical preparations of *Apolocystis* shows that the region occupied by the membranes and accompanying substance is strongly basophilic ; the same has frequently been reported for regions containing much endoplasmic reticulum. However, in the latter case the basophilia is generally attributed to fine particles[2,3] which occur close to, or in contact with, membranes of the endoplasmic reticulum. In *Apolocystis* the basophilia is due either to the membranes or to the accompanying homogeneous substance, or to both.

In some regions the membranes and accompanying substance are concentrated in the form of spheroidal or elongate bodies which appear to be similar to mitochondria seen in micrographs of other tissue. Occasionally, many dense granules of irregular outline, of the same type as seen in the base of the 'hairs', lie enclosed by the meshes of the membranous network. Larger inclusions, spheroidal in shape and about 1μ in diameter, also occur within the meshes of the network.

Within the remainder of the animal occur many large vacuoles, each with a smooth limiting membrane about 50 A. thick. Examination of light microscopical preparations stained by Best's carmine method shows that such 'vacuoles' correspond to inclusions containing glycogen (glycogen grains). Between the 'vacuoles' lie extensions of the membranous system and inclusions referred to above. Occasionally, we have observed groups of membranes and small vacuoles (= dilations or paired membranes) which together resemble the Golgi apparatus seen in other Protozoa and in various Metazoa[4].

The nucleus is variable in position and consists of two main components, a prominent nucleolus and a peripheral zone. The nucleolus is very dense in appearance being composed of numerous small, highly osmiophilic granules. Within the nucleolus are several large vacuoles. The peripheral zone of the nucleus consists of strings of osmiophilic material lying within a 'clear' matrix. The nuclear contents are bounded by a double membrane, a feature which appears to be a characteristic of nuclei throughout the animal kingdom.

We are grateful to the Wellcome Trust for a grant to purchase an electron microscope and to St. Bartholomew's Hospital and Medical College, and the University of Hull, for further financial help and facilities.

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Pogonophora in the Hardangerfjord, Western Norway

Until recently, Pogonophora were known only from the north-western Pacific and from Indonesia. All species being found in the deep sea such a limited distribution seemed unlikely, the more so as the tubes of the animals are hair-like and easily overlooked. In fact, new investigations and revision of old collections have proved that the Pogonophora are widely distributed and also occur in relatively shallow water. Thus one species is now known from the Polar Sea, and Kirkegaard found Pogonophora in the *Galathea* collections from Indonesia[1] and from the Gulf of Panama[2]. Jägersten[3] described *Siboglinum ekmani* from old collections from about 500 m. in the Skagerrak, and he also described the larva of another species from only 180 m. depth in the same area[4]. Kirkegaard[5] re-investigated the deepest parts of the Skagerrak and found more material of *S. ekmani*, and Southward[6-8] has obtained several species from the continental slope south-west of England and west of Ireland.

As the fauna of the Norwegian Deep in the Skagerrak comprises many typical deep-sea animals which also live in the deep Norwegian fjords, Pogonophora could be suspected to occur in our rich collections from the Hardangerfjord. Several samples of undetermined narrow tubes were re-investigated. Between them were found many still more slender, red-brown tubes up to 17·5 cm. long and strongly resembling those of *Siboglinum ekmani*. New dredgings in different parts of the Hardangerfjord have proved this species to be fairly abundant in depths between 396 and 840 m.

The material has been sent to Prof. G. Jägersten, who has confirmed that part of it is very similar to *S. ekmani*, whereas one animal probably belongs to another species. Thus at least two species of Pogonophora seem to occur in the Hardangerfjord.

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Utilization of Nutritive Spheres in the *Proteus* Group of *Amoebae*

In all members of the *proteus* group of *Amoebae*[1] there occur spherules of a pale blue colour to which the name 'excretion spheres' was given by early writers. This designation was changed to "nutritive spheres" by Hayes[2] in 1924. The reaction of these bodies to various reagents has been described in an appendix by Hayes to Taylor's paper entitled "*A. proteus*, some New Observations on its Nucleus Life History and Culture", and further information about them was later published by Taylor[3].

The diameter of these bodies is proportional to the age of the *Amoeba*. A quick examination of the nutritive spheres enables the observer to distinguish a newly metamorphosed *Amoeba* from an adolescent, mature or senile creature. It is necessary here to emphasize the importance to the reader of stating the age of the *Amoeba* when describing its reactions, behaviour, etc. Reaction to a certain stimulus characteristic of mature *Amoebae* may be very different from that of an adolescent. To repeat: the diameter of the nutritive spheres is a criterion of the age of the *Amoeba*, which should always be given.

In my paper[2] I used a hæmatoxylin which stained the nutritive spheres purple. In this account it was shown that during the differentiation of the spores in the adult *Amoeba* the nutritive spheres were gradually used up, so that those *Amoebae* which were full of spores could be picked out by the extreme scarcity of coloured nutritive spheres, the degree to which sporulation had proceeded being indicated by the number of nutritive spheres present.

In sections through sporulating *Amoebae*, nutritive spheres which had begun to yield up their contents looked like collapsing balls, every stage from a fully inflated to a completely collapsed sphere being found.

Recently, I have seen this phenomenon in living material. Under natural conditions the *proteus* group[1] are mature and senile in the winter months. If these mature specimens, easily identified by their large nutritive spheres (7μ), be placed in a Petri dish and kept under observation, the gradual loss of contents of the nutritive spheres, as sporulation proceeds, can be witnessed; deformed spheres of every kind, that is to say, spheres having given up varying volumes of their contents, can be picked out.

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Second Flowering in *Oryza sativa* (var. *indica*)

In India rice is normally harvested when ripe by cutting off the leaves and stems near ground-level. Shortly before this operation the field is allowed to dry. There is very little regeneration, though it is well known that rice can be propagated vegetatively by 'ratooning'. In 1958 three small plots of 5·2 square metres each at Giridih in Bihar were planted with the *aus* (rapidly maturing) variety *CH*-10 in July. Owing to the late monsoon the crop was poor. Instead of drying and cutting as usual, the plots were not allowed to dry, and the ears were plucked by hand on October 10. The plots produced a second crop which was harvested on November 23 by the usual method. Table 1 shows the yield of paddy for two harvests of the three plots.

The total yield was thus increased by 117 per cent, that is to say, more than doubled. The second crop was harvested at the same time as the *aman* (slowly maturing) rice in the neighbouring plots.

Table 1. Yield of Paddy (dry weight, gm.) for Three Plots each 5·2 square metres in Area for the First and the Second Crop

Plots / Yield	1	2	3	Total
First crop	2·3	605·4	673·0	1,280·7
Second crop	660·2	650·8	187·8	1,498·8

Regeneration was found to occur in two ways—through the formation of new tillers at the base and new branches at some nodes of the stems of the harvested plants. Both the new tillers and the new branches flowered and thus produced the second crop.

Experiments are being made this year on a large scale with numerous varieties to determine the economic value of this method of harvesting.

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Control of Leaf Senescence by Auxins

THE considerable knowledge which has accumulated over the past thirty years suggests that differentiation, growth and senescence of plant cells is closely linked to the auxin status of the tissue. Investigations by Shoji, Addicott and Swets[1] have shown that differentiating and enlarging tissues of the green leaves of Black Valentine bean contain a relatively high concentration of an extractable auxin. These levels decrease as the tissues mature and at senescence only small amounts of the auxin are detectable.

Although mature parenchymatous tissues can often be stimulated experimentally into renewed growth and cell division by supplying an auxin, the changes which take place in highly differentiated cells, such as the mature mesophyll of the leaf, are normally irreversible and their senescence and death are inevitable.

Recent work has now shown that the ageing processes in leaves can be arrested by treatment with certain chemicals, and in this way particular physiological states have been maintained for considerable periods of time. For example, Richmond and Lang[2] have shown that chlorophyll and protein breakdown and the associated loss of green colour in detached leaves of *Xanthium* can be retarded by treatment with kinetin, with a resulting extension of the life of the leaf. Person, Samborski and Forsyth[3] have found similar effects following the treatment of detached wheat leaves with benzimidazole. Brian, Petty and Richmond[4] have reported that both the natural autumnal yellowing and the subsequent leaf fall of a number of temperate deciduous trees have been delayed by spraying gibberellic acid on to the leafy branches.

From the work carried out in this Unit over a number of years it is clear that the ability to arrest physiological changes associated with leaf senescence is not a property only of kinetin, benzimidazole or the gibberellins. Synthetic auxins of the chlorophenoxyacetic acid group must also be considered. It has already been shown[5] that the natural and continuous fall in pectin methylesterase activity which occurs in the abscission zones of growing petioles of *Phaseolus vulgaris* can be prevented by treatment with 2,4-dichloro- or 2,4,5-trichloro-phenoxyacetic acids (2,4-D or 2,4,5-T) and that under these conditions, abscission and senescence of the petiolar tissues is prevented. The application of 2,4,5-T to the leaf blades of certain tropical trees has produced differential senescence within the treated leaves[6]; with suitable doses the areas immediately below the applied droplets remain permanently green and healthy while the surrounding areas become progressively yellow and senescent.

It has now been clearly demonstrated that the application of a suitable formulation of either 2,4-D or 2,4,5-T will prevent normal senescence in both attached and detached leaves of a number of temperate deciduous species. Most of the experiments have been done with *Prunus serrulata senriko* and the following procedure was adopted. During the months of October and November a drop of ethanol solution of the butyl ester of 2,4-D or 2,4,5-T was applied to the lamina on either side of the main vein to give a total dose per leaf ranging from 10 to 100 μgm. After this treatment an apparently normal yellowing and senescence occurs in the untreated areas, but in the cells of the tissues directly below the applied drop the plastids retain their chlorophyll so that, at the time of normal leaf-fall at the end of November, each treated area remains as an isolated green spot about 1 cm. in diameter surrounded by yellow tissue. With detached leaves similarly treated and kept in high humidity in the light, the untreated parts of the blade and the control leaves become entirely yellow within twelve days, while the islands of 2,4-D-treated tissue remain green until general autolysis starts some 10–20 days later.

If the leaves are treated with a radioactive butyl ester of 2,4-D, labelled with carbon-14 in the carboxyl group, the autoradiographs of the whole leaf made at various intervals after the application show that the majority of the radioactivity is initially concentrated immediately below the treated areas with only traces of activity over the remainder of the blade. This pattern of distribution remains unaltered in detached leaves, but a week after attached leaves have been treated no radioactivity can be detected in the untreated portions of the blade; activity is then confined to the areas below the drops and eventually corresponds to the areas of tissue which remain green.

The colour of the islands of green cells is not due to an immobilization of chlorophyll in an inactive form. When the leaves treated with 2,4-D are illuminated and supplied with carbon-14 dioxide a ready fixation of carbon-14 occurs in the green areas beneath the applied 2,4-D, while fixation in the surrounding yellowing tissue is negligible and of the same order of magnitude as that in a yellowing control leaf.

Respiratory studies on disks of leaf tissue have shown that the treated areas which remain green retain a relatively high oxygen uptake which equals that of an untreated green leaf, while oxygen uptake in the surrounding yellowing tissue falls progressively for many days after the application of 2,4-D and follows that in a yellowing control leaf.

Preliminary analyses of the nitrogen fractions in the treated leaves indicate that the level of alcohol-insoluble nitrogen remains higher in the green 2,4-D-treated areas than in the surrounding yellowing tissue, suggesting that there may be an effect on protein conservation similar to that described for kinetin and benzimidazole.

The evidence for the maintenance of chlorophyll and of photosynthetic activity in leaf tissue following the application of high doses of 2,4-D is of particular interest, since previous reports by Wedding, Erickson and Brannaman[7] and Akers and Fang[8] have described depressions in photosynthesis following treatment with synthetic growth-regulators. Maciejewska-Potapczyk[9] records an actual reduction of 25–40 per cent in the chlorophyll content of leaves four days after treatment with 2,4-D, and Moreland, Hill and Hilton[10] have recently found that certain phenoxyacetic acids, including 2,4,5-T, have an inhibitory effect on the photochemical Hill reaction in isolated chloroplasts.

The responses which occur in both plant growth and cellular metabolism following applications of auxins are usually considered as a departure from the control pattern. The results presented here show that, under certain conditions, 2,4-D and 2,4,5-T tend to maintain unchanged particular physiological states within the cells and thereby delay the normal changes which take place during senescence. These results thus provide a further example of the control of physiological ageing by auxins.

I am indebted to Prof. W. O. James, Dr. Mary Halloway, Dr. D. C. Smith, Mr. R. G. Powell and Dr. C. C. McCready for their co-operation in this work, and I wish to thank Prof. G. E. Blackman for his constant interest and encouragement. Further details will be published elsewhere.

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A New Nitrogen-fixing Micro-organism producing a Red Pigment

WHILE isolating strains of *Rhizobium lupini* from the nodules of *Lupinus luteus* grown on the acid sandy soil of the Nyirség area in north-eastern Hungary, I succeeded in isolating, on a *Rhizobium* medium, two red micro-organisms. These have been labelled *Pr* and *E*.3. They came from places several miles apart. The plants from which the *Pr* and *E*.3 strains derived were in a state of fluorescence and conspicuously larger than the surrounding lupins.

The new micro-organisms are spherical or ovoid cells, 4–6μ in diameter. During their growth, 2–4 spherical, strongly refringent granules appear in the cells. A daughter cell becomes detached without a sterigma developing. In aged cultures large spherical cells with diameters between 8 and 9μ can be seen in which, besides the above-mentioned granules, 5–10 additional similarly shaped but smaller granules develop.

The new micro-organisms form a slowly migrating smooth colony on agar slants, with a strong adhesion to the nutrient medium.

The cell-wall gives a good response to most of the usual stains. Carmine acetic acid stains one point of the cell-wall.

Glucose, maltose, saccharose, lactose, mannitol and salicin are decomposed by the new strains with an intensive production of acids, but without the development of gases. They produce urease and do not liquefy gelatine. They produce no hydrogen sulphide and do not reduce nitrates to nitrites. They can utilize ethanol as their only source of carbon. Placed on a bean extract containing a 3 or 6 per cent solution of ethanol they will proliferate intensively. A temperature of 16° C. ensures vigorous growth, the optimum temperature being 25–28° C. Washed off the culture medium and exposed to ultra-violet rays they give a blue fluorescence. Diffused light promotes proliferation and pigment production. They are resistant to streptomycin, which does not impair their pigment production. Low concentrations of ammonium chloride, ammonium sulphate, potassium nitrate and peptone promote growth and the development of red pigment. The *p*H of culture media adjusted to 7 is reduced by them to 5·2–4·2 within 48 hr. They grow satisfactorily and continue to produce red pigment even in media containing 0·3 per cent citric acid, with a *p*H less than 3. Placed in stab cultures and examined otherwise they were found to be obligate aerobes.

Both strains develop satisfactorily on yeast, bouillon and bean agar, and fix atmospheric nitrogen without symbiosis while producing red pigment. To be able to do so the presence of a nitrogen-source in the nutrient medium is indispensable.

The properties described justify the claim that two varieties of a new kind of *Saccharomyces* have been discovered: the only difference between them is that the red pigment produced by strain *Pr* is brighter than that produced by *E*.3. No taxonomical allocation has yet been made.

The increase in nitrogen per unit of glucose consumed has been studied in numerous experiments on a bean-soup medium which in some cases had been aerated. Results were invariably positive. The significant experiments, which were repeated several times, showed the nitrogen increase to be 2·4–5·7 mgm. nitrogen/gm. glucose. Culture flasks through which air had been passed gave the higher value.

The results obtained from four different treatments (each repeated three times) are given in Fig. 1.

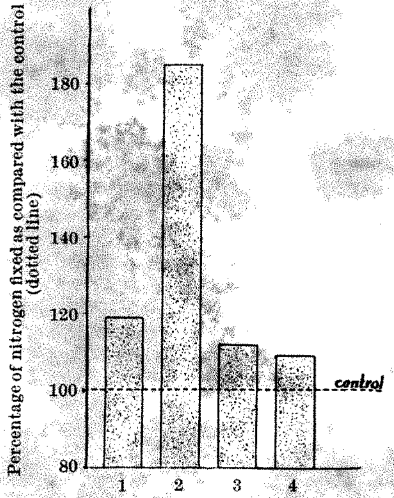

Fig. 1. (1) Bean soup (a 5 per cent decoction of white beans containing 2 per cent glucose, 0·3 per cent sodium chloride and 0·2 per cent potassium dihydrogen phosphate). Aerated during cultivation with a vacuum pump and sterile air. 40 ml. per culture flask. (2) 40 ml. of bean soup added to 80 ml. of 0·3–0·8 mm. diameter sterilized quartz sand. (3) 40 ml. of bean soup added to natural washed, finely granulated, sterilized sand. (4) As (3), but unsterilized. The bean soup was inoculated with 1 ml. of suspended *Pr*-strain. Sterilization was carried out in an autoclave for 20 min. at 2·5 atm. Nitrogen fixed was determined by Kjeldahl's method

That the value obtained in (4) is inferior to that in (3) is presumably due to the presence of antagonistic micro-organisms in the unsterilized sand as, otherwise, there was no difference between the two soils.

There was a correlation between the degree of nitrogen fixation and the red colour. This suggested that the red pigment may have a role in fixing atmospheric nitrogen similar to that of leghæmoglobin, which occurs in the nodules of leguminous plants and is known to be involved in symbiotic nitrogen fixation. The determination of a relationship between leghæmoglobin and the red pigment would be very useful in elucidating the chemical mechanism of atmospheric nitrogen-fixation.

Investigations with this end in view have been started in the Institute for Organic Chemistry at Szeged, and experiments performed under the supervision of G. Fodor by B. Matkovics produced the following results: (1) The red colour of the pigment produced by strain *Pr* is due to a hæmoprotein related to hæmoglobin as shown by the ultra-violet spectroscopic data of J. Hires; (2) a porphyrin ester from leghæmoglobin has been prepared[1].

Investigations on the exact structure of the pigment from strain *Pr* are being carried out by G. Fodor and co-workers in the Stereochemical Laboratory of the Academy, Budapest.

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Preparation of Autoradiograms for Electron Microscopy

FREQUENTLY when examining autoradiograms of biological specimens there is a need for resolution such as can be obtained with the electron microscope. A technique for preparing autoradiograms for electron microscopy has been reported by Liquier-Milward[1]. The method described here has the advantage of being somewhat simpler in that nuclear emulsion is applied directly to the specimen grids, and the method is suitable for use with ultra-thin sections. Although only results obtained with yeasts and the alpha-emitter polonium-210 are described, other isotopes and biological specimens can be used.

Yeast cells, previously suspended in a polonium-210 solution, were fixed with 2 per cent osmium tetroxide containing 0·8 per cent sodium chloride[2]. The fixed cells were dehydrated in a graduated series of ethanol concentrations and embedded in methacrylate. Good results were obtained with a mixture of four parts N-butyl methacrylate and one part methyl methacrylate[3]. Ultra-thin sections were cut with a Porter–Blum microtome, transferred to carbon-coated specimen grids, and allowed to dry thoroughly. All subsequent steps were carried out under light filtered through a Wratten series *OA* filter. Alpha-sensitive Eastman Kodak *NTA* emulsion in gel form (obtained through the courtesy of the Eastman Kodak Co., Rochester, N.Y.) was heated at 45° C. until fluid. A drop of the liquid emulsion, either full strength or diluted 1 : 1 with distilled water, was transferred to a clean glass slide. Specimen grids were coated by touching them to the drop of emulsion. Occasionally the yeast sections floated off when contact was made with the emulsion. This was due to insufficient drying of the grids before emulsion was applied. After coating, the grids were placed in a light-tight box containing a small vial of anhydrous calcium sulphate and exposed for 3–4 weeks at 4° C. The autoradiograms were developed for 15 min. in Eastman Kodak *D*-19 developer, fixed in acid fixer for 5 min., washed thoroughly in running tap water, and finally rinsed in distilled water. After drying they were examined with an *RCA EMU-2C* electron microscope.

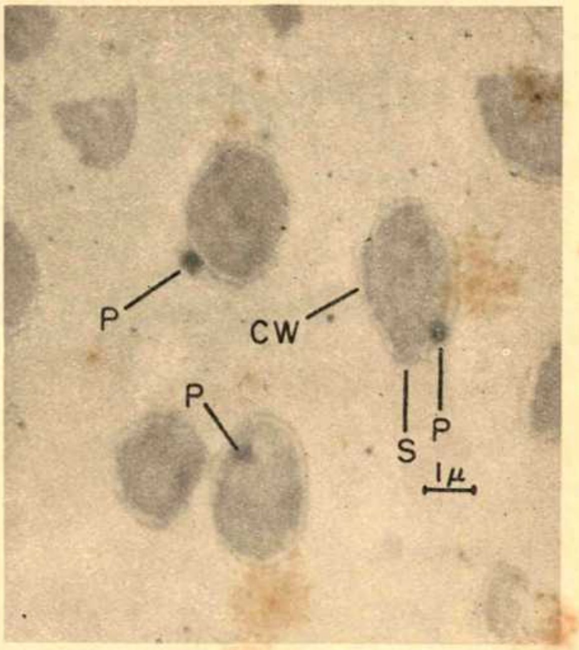

Fig. 1. Electron micrograph of autoradiogram showing distribution of polonium-210 on yeast cells. *P*, Polonium track; *CW*, cell wall; *S*, bud scar

Typical results are shown in Figs. 1 and 2. It is apparent that the emulsion obscured some cellular detail; however, in spite of this, good autoradiographic resolution of the location of polonium-210 in the cells was obtained. There was no evidence that

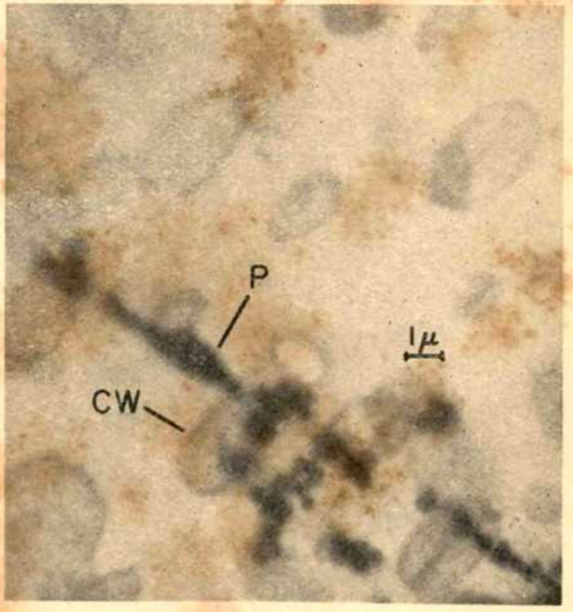

Fig. 2. Electron micrograph of an alpha track from polonium-210 on yeast cells. Key as in Fig. 1

sectioning caused displacement of the radioactivity. Due to the thinness of the film, only those particles which travelled at angles estimated to be less than 1° from horizontal were recorded as typical alpha tracks. Actually, this was an advantage since long tracks did not give the autoradiographic resolution that shorter ones did. A comparison of the figures illustrates this. In Fig. 1 the location of polonium-210 is much better defined than in Fig. 2. Radioactivity was almost entirely located on the surface of the cells, although a few were found to have polonium-210 in the cytoplasm (Fig. 1). This suggests that yeasts are nearly impermeable to this element. Further details on the distribution of polonium-210 and other heavy metals in yeast cells will be reported elsewhere.

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PHYSIOLOGY and BIOCHEMISTRY

Use of 'Tremorine' for screening Anti-Parkinsonian Drugs

'TREMORINE' (1 : 4-dipyrrolidine-butyne) has been proposed[1,2] as a test drug against which anti-Parkinsonian agents may be screened and evaluated by their effect on the tremor induced by 'Tremorine' in mice. We have investigated the action of the compound in toads, mice, rats and guinea pigs; trials with larger animals, dogs and cats, were restricted by the shortage of 'Tremorine'.

The incidence and intensity of the symptoms caused by an effective, non-lethal dose of 'Tremorine' (*LD*5 or lower) varied with the species. Toads survived high doses (150 mgm./kgm.) without showing any constant characteristic symptoms other than transient excitation and occasional 'yawning', possibly indicating some discomfort in the respiratory passages. The mammals tested all showed a similar pattern of response. The *LD*50 for mice was of the order of 65 mgm./kgm. subcutaneous and 3–5 mgm./kgm. intraperitoneal; for rats 75 and 15 mgm./kgm. respectively, for guinea pigs 25 and 2·5 mgm./kgm. respectively. The effective dose, causing characteristic symptoms persisting for a few hours, was about one-quarter of the *LD*50. This dose was high enough to cause an occasional death. All animals tested exhibited within 15–30 min. of 'Tremorine' injection salivation, diarrhœa, occasional or persistent fine tremors of fore-limbs and head at the rate of 7–10 per sec., occasional single jerks or even convulsions, hypothermia and some analgesia. The present investigation was mainly concerned with the Parkinsonian-like tremors, and hypothermia was prevented by keeping the animals warm. The analgesic effect in mice has been dealt with by Chen[3] and electroencephalographic studies in cats have been made by Kaelber and Correll[4].

At the height of the drug effect, the animals were visibly ill, stretched out flat and unwilling to move, though responsive to stimuli and apparently fully aware of their surroundings. When moving, their limbs were often extended and stiff. Strutting of the fore-limbs or biting on the food tins or the wires of the cage may possibly be interpreted as behaviour aimed at negating the tendency to tremors.

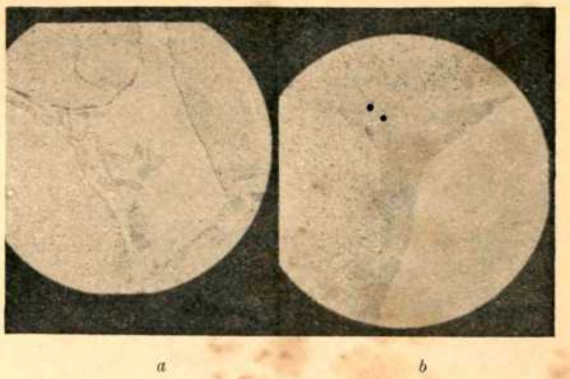

Fig. 1. From guinea pig killed 160 min. after injection of 70 mgm./kgm. 'Tremorine' subcutaneously. *a*, Intraventricular hæmorrhage; *b*, hæmorrhage on the surface of the cortex between gyri. Photomicrographs by courtesy of Dr. J. Mackiewicz

Typical persistent tremors were seen only in mice. In guinea pigs profuse salivation was most marked; in general, these animals appeared to be more prostrated than mice and tremors could often be demonstrated only when the animal was induced to move. The most impressive sign in rats was sanguineous lachrymation together with salivation and diarrhœa of the same nature as that caused by 0·5 mgm./kgm. carbamylcholine intraperitoneally.

The incidence of death at doses less than the *LD*50 was variable. Some animals died within 30 min. of injection, some died hours later after they appeared well on the way to recovery, while others died after 24–30 hr. in a prolonged coma, or in their sleep. Of those who died early, about 30 per cent had sudden, strong convulsions just before death, while the rest showed merely increasing sluggishness and weakness. Some animals recovered after they had already been recorded as dying. On post-mortem examination almost all animals, whether they died early or late, had injected brain vessels, and often visible hæmorrhages in the hemispheres or small blood clots in the ventricles (Fig. 1), 80 per cent had gross hæmorrhages as well, mainly subdural at the base of the brain or the brainstem, intrapericardial, intrapleural or intraperitoneal. A few retroperitoneal hæmorrhages were observed. It appeared that convulsions were present mainly in animals with cerebral hæmorrhages, but were absent with other internal hæmorrhages. Some intestinal hæmorrhages were also observed.

Repeated administration of sublethal doses of 'Tremorine' at intervals of 24–48 hr. did not produce convincing evidence of tolerance or cumulation, but it seemed that tremors and other motor disturbances were reduced while salivation and diarrhœa remained unaffected. (For this observation the animals were used only once, and kept at room temperatures above 16° C. throughout the experiment and the observation time.)

Atropine was found to be the most potent of all antagonists tried. In guinea pigs (*LD*50 of atropine sulphate about 400 mgm./kgm. intraperitoneally) 1–2 mgm./kgm. intraperitoneally prevented all symptoms if injected 20–30 min. before 'Tremorine', and abolished them within 10–15 min. if administered after full development of the 'Tremorine' symptoms. The corresponding dose for the amino-alkyl ester 'Parpanit' was 25 mgm./kgm., and for the amino-alcohol 'Kemadrine' 17 mgm./kgm. The same effect was observed in mice. In rats no difference in the effect of antagonists could be noted whether the salivation and lachrymation were induced by 'Tremorine' or by carbamylcholine.

Everett's observation that the quaternary amino-alkyl ester 'Methantheline' (Banthine) in mice antagonizes the secretory symptoms preferentially without noticeably affecting the tremor was confirmed. The quaternary atropine-homologue propionylatropine-methylnitrate, 2–3 mgm./kgm. intraperitoneally, showed the same preferential antagonistic effect in mice, rats and guinea pigs. It must, however, be noted that in all animals recovering from 'Tremorine' alone, the tremors and other muscular symptoms persisted after diarrhœa and salivation had ceased, and could often be demonstrated on the following day when the animal had in all other respects completely recovered.

Another atropine homologue, tiglyl-pseudotropine ('Tigloidine'), which in clinical trials[5] had proved to be effective against Parkinsonian and related extrapyramidal disorders while lacking the *p*-sympathicolytic action of atropine, showed in weak doses only doubtful antagonistic effects against 'Tremorine'. At high doses of both compounds it even appeared that their toxic effects were potentiated; in some experiments all animals, mice, rats or guinea pigs which had received the combined medication convulsed and died, while the controls survived; the 'Tigloidine' controls without any noticeable symptoms, and the 'Tremorine' controls with the usual diarrhœa, salivation and muscular disturbances.

On these observations it does not appear to be justified to separate the tremor effect induced by low doses of 'Tremorine' in mice from the diarrhœa, salivation and other effects seen in all animals tried. These latter effects are notably absent in cases of Parkinsonism and related disorders. Furthermore, in animals practically recovered from 'Tremorine', tremors can usually be elicited if the animal is disturbed, while the typical Parkinsonian tremor is a tremor at rest. It would seem that 'Tremorine' is best classed with the group of *p*-sympathicomimetic drugs which all cause to a varying degree increased glandular secretion, gastro-intestinal motility and muscular over-activity ranging from tremors to convulsions. To all of these atropine and related compounds are common and highly effective antagonists. The fact that these antagonists are beneficial in Parkinsonism and related disorders may indicate that there is some relationship between these disorders, but it does not prove or even suggest that they are identical. It is doubted whether the 'Tremorine' and related tests can justifiably be presented as tests for anti-Parkinsonian drugs.

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Excessive Uric Acid Production in the Human induced by 2-Ethylamino-1,3,4-thiadiazole

An excessive endogenous synthesis of uric acid is present in a substantial portion of patients with gout[1]. The precise nature of the metabolic defect responsible for such excessive production is not known, but may be the result of a defective homœostatic mechanism for control of purine synthesis. Evidence for the existence of such a mechanism in the normal human has come from the observation[2] that the simultaneous administration of 4-amino-5-imidazolecarboxamide suppresses *de novo* purine biosynthesis from glycine-^{15}N. Factors affecting uric acid synthesis in the human are therefore of special interest in regard to the study of gout.

The administration of 2-ethylamino-1,3,4-thiadiazole to human subjects as treatment for cancer results in a several-fold increase in both the excretion of uric acid in the urine and the serum urate-levels[3]. An increased purine biosynthesis was proposed to account for this observation, but an increased urate production and an elevation of serum urate has also been observed to accompany lysis of leukæmia cells during therapy[4], and destruction of other tissues could conceivably give similar results. A definitive experiment to rule out one of these alternative explanations was needed.

We have confirmed the original observation that the administration of ethylaminothiadiazole does result in a substantial increase in serum uric acid-levels accompanied by a two- to five-fold increase in urinary uric acid excretion. By measuring the incorporation of glycine-1-^{14}C into urinary uric acid in the presence and absence of ethylaminothiadiazole, we have been able to demonstrate that this increased uric acid excretion is accompanied by an increased incorporation of carbon-14 into uric acid (Fig. 1). Since uric acid arising primarily from degradation of tissue purines would tend to dilute the isotope in newly formed purines and give rise to a lower specific activity of uric acid, the present findings indicate a marked stimulation in the *de novo* synthesis of purines as a result of ethylaminothiadiazole action. The cumulative incorporation of the isotope into uric

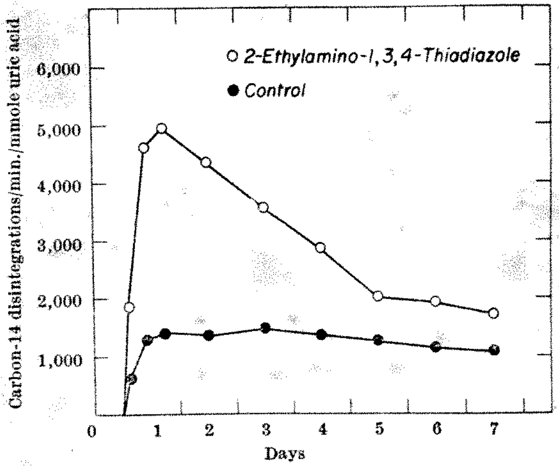

Fig. 1. Increased incorporation of glycine-1-^{14}C into urinary uric acid resulting from the administration of 2-ethylamino-1,3,4-thiadiazole to a non-gouty subject. 5 μc. of glycine-1-^{14}C was given orally at the beginning of each study and uric acid was isolated from the urine (ref. 2). A total of 350 mgm. of ethylaminothiadiazole hydrochloride was given in divided dose over a two-day period beginning one day before the second study

acid over a seven-day period was more than four times that observed in a similar period in the absence of ethylaminothiadiazole. The pattern and extent to which glycine-1-^{14}C was incorporated into uric acid in the presence of ethylaminothiadiazole with a maximum incorporation on the first day is very similar to the pattern of incorporation observed in many gouty subjects[5].

Some of the biological effects ascribed to ethylaminothiadiazole can be prevented by the simultaneous administration of nicotinamide. The carcinostatic action in experimental tumours in mice is diminished by nicotinamide[6]. We found that the increased serum urate-level and the increased uric acid excretion in the human could be completely prevented by administering a dose of nicotinamide four times the dose of ethylaminothiadiazole. This antagonism by nicotinamide was not apparent at equal doses of nicotinamide[3].

The increase in purine biosynthesis induced by ethylaminothiadiazole in the non-gouty human provides additional evidence favouring the view that purine biosynthesis is normally governed by a regulatory mechanism. A detailed explanation of the action of this drug should be of considerable value in defining the factors which normally operate to control the rate of purine biosynthesis in the human.

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Enzyme Activity in the 'Isolated' Colon

DURING the course of physiological and histological studies on the intestine of the cat, an opportunity was presented for comparing the histochemical activity of the enzymes alkaline phosphatase and non-specific esterase in the colon before and after it had been isolated from the small intestine for varying periods of time following the operation of ileostomy.

In eight cats, the terminal half-inch of the ileum together with the proximal one inch of the colon were removed in one piece, and after the contents of the colon had been expressed the cut ends of the colon and ileum were closed. A special cannula was inserted into the terminal ileum through a separate incision in its wall, and drained into an external receptacle. From the portion of the proximal colon removed at operation two small pieces were excised; one was fixed in cold 80 per cent alcohol for the histochemical demonstration of alkaline phosphatase by means of Kabat and Furth's[1] modification of Gomori's[2] 'cobalt sulphide' technique, and the other was fixed in cold absolute acetone for the histochemical demonstration of non-specific esterase by means of a modification[3] of Gomori's[4] 'Tween' technique, using 'Tween 40' as the substrate.

Table 1

No.	Before ileostomy		After ileostomy	Days
1	*A.P.*	+(+)	++	3
	Est.	+(+)	++	
2	*A.P.*	+	+(+)	5
	Est.	+(+)	+(+)	
3	*A.P.*	+	(+)	5
	Est.	(+)	(+)	
4	*A.P.*	+(+)	++	5
	Est.	+	++	
5	*A.P.*	(+)	++	5
	Est.	(+)	++	
6	*A.P.*	+(+)	++	5
	Est.	+(+)	++	
7	*A.P.*	+(+)	++	8
	Est.	++	++	
8	*A.P.*	+(+)	+	10
	Est.	(+)	(+)	

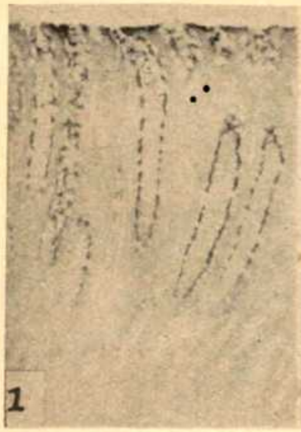
A.P., Alkaline phosphatase; *Est.*, non-specific esterase. The signs (+), +, +(+), ++ indicate the intensity of the enzyme activity.

After periods ranging from 3 to 10 days, the animals were killed, and pieces of tissue were removed from near the sutured end of the proximal colon for histochemical study of the activity of alkaline phosphatase and non-specific esterase, which was then compared with the activity shown in the biopsy specimens.

The histochemical reaction for alkaline phosphatase is particularly intense in the large intestine of the cat, and is of about equal intensity throughout its length[5]. The reaction is present in the intestinal contents, in the surface epithelium and in that of the crypts, extending into the latter for two-thirds or more of their length, then gradually fading in their deeper parts; this reaction occurs at the striated border of the cells of the surface and crypt epithelium and sometimes also in granules in the distal part of the cell cytoplasm. In addition, the reticular fibres around the crypt bases are positive. Non-specific esterase, as demonstrated by the 'Tween' technique, is localized in the cytoplasm of the epithelial cells lining the intestinal surface and approximately the upper one-third of the crypts, but the intestinal contents do not react[6].

Comparison of the enzyme activity in the specimens taken from the proximal colon before and after ileostomy was made by incubating all the sections in the same substrate bath for the same period of time. The reaction for alkaline phosphatase is so intense in the cat's colon that, to make this comparison, a very short incubation period had to be employed: after several trials, it was found that 2 min. was a suitable period to use. In the case of non-specific esterase, a long incubation period is needed with the 'Tween' technique to bring out a reaction; a period of 48 hr. was used, but, even after this time, differences in intensity of reaction were apparent.

The results of the investigation are summarized in Table 1. It is seen that, with the exception of two cases (Nos. 3 and 8), the reaction for alkaline phosphatase actually increased after ileostomy. Following the very short incubation period used, the histochemical reaction was somewhat incomplete, even in this strongly reacting tissue; it first appeared at sites of greatest activity, namely, in the middle and upper parts of many crypts, areas of the surface epithelium and sometimes in the contents within the crypts and intestinal lumen. Any increase in enzyme activity was shown by a heavier deposit of cobalt sulphide in



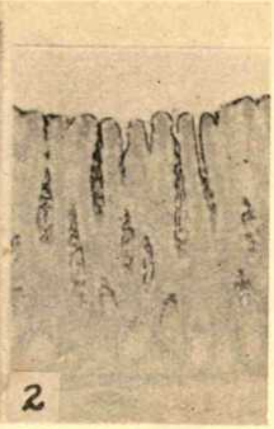


Fig. 1. Proximal colon, cat. Alkaline phosphatase reaction before ileostomy. 2 min. incubation. (× 75)

Fig. 2. Alkaline phosphatase reaction 5 days after ileostomy. The reaction has increased in extent and in intensity. Note shrinkage of the mucous membrane. 2 min. incubation. (× 75)

the reactive areas, and by an extension of the areas of reaction in the surface and crypt epithelium. An extension of the reaction into the deeper parts of the crypts, where the reaction is normally weaker than in the upper parts, was a particularly useful index of increased enzyme activity. Comparison of Fig. 1 with Fig. 2 (sections from No. 5 in Table 1) illustrates the difference in activity encountered before, and five days after, ileostomy.

Regarding non-specific esterase, it will be seen from Table 1 that in no case was there a decrease in enzyme activity after ileostomy ; in four cases there was no obvious change, but in the other four (Nos. 1, 4, 5 and 6) there was actually an increase in activity.

It is concluded that, within the colon of the cat after 'isolation' by means of the operation of ileostomy, there is no diminution in the activity of the enzymes alkaline phosphatase and non-specific esterase, even after five or more days ; on the contrary, the activity tends to increase.

It has been shown experimentally that alkaline phosphatase is secreted by the dog's colon[7]. The present histochemical results indicate that this is true for the cat, since the contents in the intestinal lumen and in the crypts are positive before and after ileostomy. However, the results show that the inflow of ileal contents is not a necessary factor either in maintaining the activity of the enzyme within the lining epithelium or in stimulating its continuous secretion. It is possible, however, that the quantity of alkaline phosphatase *secreted* is less in the 'isolated' colon, and that the increased activity in the epithelium indicates some degree of enzyme storage in the resting colon.

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Distribution of Haptoglobins in Native Venezuelans

HAPTOGLOBINS are globulins present in normal human plasma which are capable of combining and carrying hæmoglobin. First detected by Polonovsky and Jayle[1] in 1938, they became the object of detailed studies, mainly by French authors[2]. Smithies[3], in 1955, studying normal human serum by zone electrophoresis in a starch gel supporting medium, showed that it was possible to differentiate three groups easily when a certain amount of hæmoglobin was added to the serum. It was later demonstrated that this polymorphism was based on electrophoretic differences in the haptoglobins[4].

In 1958, Allison, Blumberg and Rees[5] studied the distribution of haptoglobins in English subjects, Spanish Basques and Negroes from Nigeria. By comparing these results with previous studies[6,7] made on Canadian and United States subjects and negroes from Liberia and the Ivory Coast[7], they concluded that the distribution of haptoglobins might well have anthropological significance. Since the Venezuelan population is derived mainly from various Indian racial stocks, different European groups (especially Basques and other Spanish branches) and African Negroid populations, a study of such a population should help prove such an assumption. The present communication gives the first results obtained by studying the distribution of different types of haptoglobins in the native population of Venezuela.

A study was conducted on 208 adult persons, aged 18–50, apparently normal, most of whom were voluntary donors of the Hospital Universitario de Caracas Blood Bank. The majority was from Caracas and the rest came from nearby districts and such distant places as San Cristóbal (Estado Táchira), San Fernando (Estado Apure) and Güiria (Estado Sucre). Since donors are generally male, only 27 female subjects were studied.

Blood was obtained by venipuncture and left clotting for 2–3 hr. Sera not immediately used were kept frozen until the time of use, when enough hæmoglobin solution was added to saturate haptoglobins.

In order to distinguish the various groups of haptoglobins, zone electrophoresis in a starch gel was used, according to Smithies's method[6], with slight modifications which will be described separately. After electrophoretic migration the starch gel slab was divided horizontally into two halves. One of them was stained with amidoschwarz 10*B* and the other with benzidine[8]. By this method it was easy to classify the right type of haptoglobin for each sample, and in order to check this classification those pertaining to one group were again studied together. This also gave a comparative evidence of previously described minor differences in subjects having the same phenotype[6,8,9].

Both the ABO and Rh blood group systems were determined by standard techniques.

The material studied gave a frequency of 27·40 per cent for phenotype 1–1, 17·79 per cent for 2–2 and 54·81 per cent for 2–1. This corresponds to a frequency for gen Hp^1 of 0·54805 and for gen Hp^2 of 0·45195. The χ^2 test for 'goodness of fit' was 0·011. With 1 degree of freedom, P is 0·91.

No relation was found, in analysing our results (Table 1), between haptoglobins and blood groups. This agrees with other authors[10,11].

Table 2 shows the distribution of different types of haptoglobin in the populations hitherto studied, to

Table 1. Distribution of Haptoglobins according to Sex, ABO and Rh Blood Group Systems

Haptoglobin phenotypes	No.	Sex (per cent)		ABO (per cent)				Rh (per cent)	
		Male	Female	O	A	B	AB	+	−
Hp 1–1	57	87·72	12·28	42·10	38·60	12·28	7·02	96·49	3·51
Hp 2–1	114	89·47	10·53	54·39	29·82	11·4	4·39	90·35	9·65
Hp 2–2	37	78·38	21·62	48·65	45·95	2·70	2·70	86·49	13·51

Table 2. Distribution of Haptoglobin Types in Various Populations

Population	Reference	No. tested	0–0		1–1		2–1		2–2	
			No.	(per cent)	No.	(per cent)	No.	(per cent)	No.	(per cent)
Caucasoid :										
Canadian (Toronto)	6	49	0	0	10	21·1	25	50·5	14	28·4
American (Chicago)	7	54	0	0	16	11·1	29	53·7	19	35·2
Swedish (Lund)	11	46	0	0	7	15·0	23	50·0	16	35·0
British (Oxford)	5	218	6	2·7	22	10·1	121	55·5	69	31·7
Basque	5	107	1	0·9	15	14·0	49	45·7	42	39·3
Negroid :										
Africans (Liberian and Ivory Coast)	7	142	0	0	69	48·7	60	42·3	13	9·1
African (Nigeria)	5	99	32	32·3	53	53·5	11	11·1	3	3·0
Hybrid :										
Venezuelan (Caracas)	—	208	0	0	57	27·40	114	54·80	37	17·80

which our own results have been added. When an anthropological separation is made, the material investigated by us appears to be the first hybrid population studied.

It appears from this Table that our results are fundamentally different, in many respects, from those obtained by other authors. The frequency obtained for phenotype 1–1 (27·40 per cent) is much higher than that obtained for Caucasoid populations but lower than that of Negroids. This incidence might indicate in what percentage the African race enters into our native population. On the other hand, the frequency of phenotype 2–2 found in the Venezuelan population (17·79 per cent) is much higher than that found in African populations but lower than that of Caucasoids, which might indicate the participation of the European element in our hybrid population. Our results seemingly confirm the anthropological importance of haptoglobin frequency. Since the Indian population has not been studied before it has not been included. It is now being investigated and will be the subject of a further report.

It is of importance that the presence of phenotype 0–0 was not noticed in our material. This phenotype was not originally described by Smithies[6], but its existence was postulated by Allison, Blumberg and ap Rees[5] in their studies of samples from Nigeria, and also by Harris, Robson and Siniscalco[12] in their studies of 107 families. Keeping in mind the high percentage in which the African factor enters into the constitution of the present native population of Venezuela, this negative result is of primary importance since it indicates that the African populations taken to Venezuela in the days of the slave trade may have been biologically different from the present population of Nigeria. If future investigations should confirm the absence of this phenotype in the normal population of Venezuela or any other South American country, these results would confirm those of Sutton *et al.*, who apparently found no individual differences from the three phenotypes described by Smithies[3,6]. This is contrary to the idea of Allison *et al.* that the series of Sutton *et al.* possibly included subjects of group 0–0 in group 1–1. If this explanation is rejected, one would have to conclude that both the samples from Nigeria examined by Allison *et al.* and the material studied by Harris *et al.* comprised persons who for some subclinical process (hæmolytic anæmia, pernicious anæmia, hepatitis, etc.) showed a temporary absence of haptoglobins (acquired ahaptoglobinæmia) instead of a permanent absence (congenital ahaptoglobinæmia). Careful analysis of the results of Allison *et al.* (Table 2) seems to show that the great proportion of phenotype 0–0 found reduces the frequency of phenotype 2–1. This phenotype, with the most haptoglobins, is more easily made to disappear by any of the pathological processes mentioned above.

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Pathways and the Physiological Site of Anserine Formation

It is clear from *in vivo*[1] and *in vitro*[2] studies that vertebrate skeletal muscle contains an enzyme that can condense 1-methylhistidine and β-alanine (in the presence of magnesium and adenosine triphosphate) to yield anserine. However, two other paths of anserine biosynthesis have been suggested[1]: β-alanyl transfer from carnosine to methylhistidine, and the direct methylation of carnosine. The former possibility has not yet been investigated. The latter alternative is the subject of the present communication. While methyl-labelled methionine was shown to supply effectively the methyl group of anserine[3,4] *in vivo* it was not evident from such experiments whether N-methylation occurred at the histidine or carnosine stage, nor was the physiological site of anserine formation revealed.

The investigations of Cantoni[5] and of Stekol, Anderson and Weiss[6] have disclosed that S-adenosylmethionine is the direct methyl group donor in the synthesis of creatine (from guanidoacetic acid) and choline (from dimethylaminoethanol) in the liver. It was of interest, accordingly, to determine whether the activated methionine derivative could likewise transfer its methyl radical to histidine or carnosine in the presence of tissue preparations. For this purpose we prepared S-adenosyl-L-methionine, labelled in its methyl with carbon-14, by a biosynthetic method[6]. An extract of chick pectoral muscle[2], found to be active in the biosynthesis of carnosine and anserine, was tested under conditions similar to those employed for the synthesis of choline and creatine by liver homogenates[6], except that our substrate concentrations were somewhat higher. Following a 2-hr. incubation at 37° C. (Fig. 1), the protein was precipitated by addition of 1·5 ml. of ethanol to the reaction mixture, and heating to boiling. After centrifugation, aliquots of the supernatant solution were subjected to paper chromatographic analysis (Whatman No. 1). The solvent was *t*-butanol–formic acid–water (70 : 15 : 15). After 24 hr. the methylhistidine and anserine regions were about 3–5 cm. from the origin, while the excess isotopic methionine and its adenosyl derivative (actually decomposed, apparently to S-methyladenosine) migrated much farther along the paper. The desired radioactive areas were cut out and measured in a windowless gas-flow Geiger counter. All values were corrected for the small background radioactivities found in parallel experiments with inactivated enzyme preparations. Fig. 1 shows that even in the absence of non-labelled substrate about 1 per cent of the carbon-14 of adenosylmethionine was used for transmethylation. This result can very likely be attributed to the considerable concentration of carnosine in the muscle extract employed. With the addition of excess histidine, the utilization of adenosylmethionine reached 2 per cent; while a value of 3 per cent was attained when the concentration of added carnosine was 9 μmoles/ml. It can be seen that methionine itself was ineffective for methylation. Apparently this amino-acid was not activated under the conditions employed.

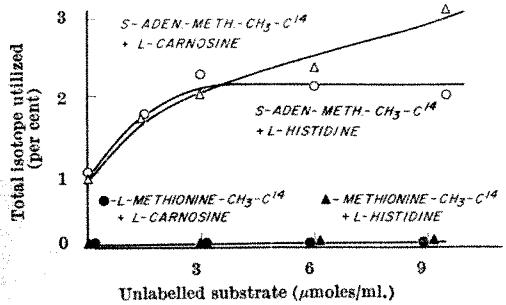

Fig. 1. Comparison of methione and its adenosyl derivative as methyl donors for histidine and carnosine. The incubation mixture (0·5 ml. final volume, *p*H 7·4) contained 0·3 ml. of centrifuged 1 : 4 muscle homogenate, histidine or carnosine in varying concentrations, and either L-methionine-CH_3-^{14}C or S-adenosyl-L-methionine-CH_3-^{14}C (each with an activity of 0·1 mc./m.mole) at a level of 3·5 μmoles/ml.

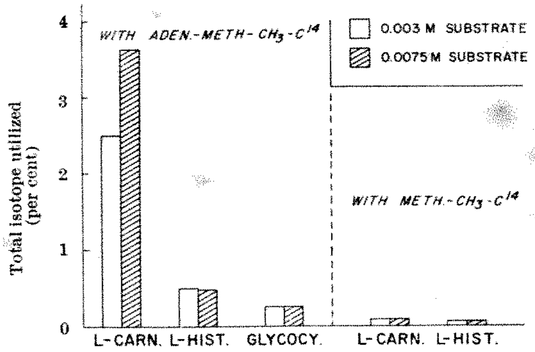

Fig. 2. Relative rates of methylation of histidine and carnosine by ethanol-precipitated protein fraction of muscle. The incubation mixture (0·5 ml.) contained 8 mgm. protein and 3·5 μmoles labelled methylating agents per ml., in addition to histidine or carnosine. The conditions of incubation and of subsequent analysis were those of Fig. 1 except that *n*-butanol–ethanol–water (4 : 1 : 1) was used for the chromatographic isolation of creatine (found 2–4 cm. from the origin after 24 hr.)

Similar results were obtained (Fig. 2) when a protein fraction of chick pectoral muscle extract, precipitated between 20–60 per cent ethanol concentration[7], was used as source of enzyme. The rate of methylation of carnosine relative to that of histidine is accentuated in Fig. 2, as compared with the corresponding ratio with the crude muscle extract. Here again, when free isotopic methionine was used, no significant radioactivity was found in the methylhistidine or anserine regions of the chromatograms. Our highest values obtained with muscle are comparable in magnitude to those for creatine and choline synthesis with liver homogenates (about 4–5 per cent utilization of adenosylmethionine in 2 hr.)[6].

The results with muscle enzyme were confirmed by the use of isotopic histidine and carnosine, together with unlabelled S-adenosylethionine. The availability of these compounds and the ease of chromatographic separation of ethylated products (as compared with methylated) from the parent histidine and carnosine suggested the experiment of Table 1. Following incubation, chromatography was performed with 2 : 1 pyridine/water for 24 hr. Histidine and carnosine migrated 19–21 cm., while ethylhistidine and ethylcarnosine were located at 24–26 and 25–27 cm., respectively, from the origin. (Synthetic 1-ethylhistidine[7] was used as a reference standard.) Because of the very soft β-rays of tritium it was necessary to elute the ethylcarnosine region from the paper, and to evaporate the eluate on a planchet, in order to measure accurately the radioactivity (in the gas-flow counter). Table 1 shows that, as in the methylation experiments, carnosine was N-alkylated more readily than histidine.

In experiments performed with chick liver homogenates we could not detect significant utilization of labelled adenosylmethionine for transmethylation of

Table 1. ADENOSYLETHIONINE AS AN ALKYLATING AGENT FOR HISTIDINE AND CARNOSINE

The conditions were those of Fig. 2, except that the incubation mixture contained 2 μmoles/ml. of non-isotopic S-adenosyl-L-ethionine and 3·5 μmoles/ml. of either DL-histidine-2-^{14}C (0·5 mc./m.mole) or L-carnosine-^{3}H (about 1 mc./m.mole). The latter compound was prepared by tritium-recoil labelling (ref. 8), and purified by paper chromatography with 2 : 1 pyridine–water

Isotopic substrate	Percentage of total radioactivity utilized for transethylation
L-Histidine-2-^{14}C	0·75
L-Carnosine-^{3}H	2·15

carnosine or histidine. It had been previously found that liver slices were incapable of synthesizing carnosine and anserine from their constituent amino-acids[9]. Hence it appears likely that skeletal muscle is the tissue concerned with both peptide bond formation and the methylation process. Although our results indicate that carnosine is methylated to a greater extent than is histidine, both *in vivo* and *in vitro* experiments show that methylhistidine condenses more readily with β-alanine than does histidine. Thus it is difficult to decide which path is the major one for anserine formation in the animal.

Liver is commonly regarded as the organ concerned with the methylation of guanidoacetic acid. However, since creatine is abundant in muscle but not in liver, it seemed of interest to determine whether muscle tissue could also form creatine from its precursor. Fig. 2 shows that this process was negligible in circumstances which promoted relatively rapid methylation of carnosine by adenosylmethionine. If it is assumed that the conditions employed for the detection of creatine synthesis were optimal, the results suggest that the transmethylating system of muscle is rather restricted in its specificity, and may function primarily in the formation of anserine.

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A New Hæmagglutinating Substance in the Gm System, Anti-Gm

A SYSTEM of inherited serum groups has been described by Grubb and Laurell[1]. Sera from certain patients with rheumatoid arthritis agglutinated Rh-positive red cells which had been coated with selected incomplete anti-D. The agglutination was inhibited by sera from about 60 per cent of normal individuals, who were said to be Gm(a+) because the inhibiting substance was located in the gamma-globulin fraction of serum. This substance was inheritable, determined by the gene *Gm*^{a}, which expressed itself in single or double dose. The corresponding allele was called *Gm*.

Among 320 unrelated Norwegians, the following frequencies were found[2]:

Phenotypes	Genes
Gm(a+) 194 (60·63 per cent)	Gene *Gm*^{a} 0·3726
Gm(a−) 126 (39·37 per cent)	Gene *Gm* 0·6274

We investigated sera from 65 patients with rheumatoid arthritis presenting a positive Waaler-Rose's test, and found one serum (J.K.) which contained a substance antithetic to anti-Gm^a.

Group O red cells of genotype C+ D+ E+ c+ were coated with a selected sample of incomplete anti-D. The anti-D serum was of type Gm(a−). After washing, the cells were agglutinated by serum J.K. diluted up to 1 : 256, giving a score[3] of 29. The reactions were run on a slide as previously described[2], and the degree of agglutination was read microscopically. The agglutination was inhibited by pooled human gamma-globulin and by 97 (81·5 per cent) of 119 sera from unrelated individuals. For typing, the rheumatoid serum was set up in serial twofold dilutions. To one drop of each dilution one drop of the serum to be tested (diluted 1 : 8) and one drop of a 0·3 per cent suspension of coated red cells were added. Most of the sera (81·5 per cent) inhibited the agglutinating substance of serum J.K., as shown by reduction of agglutination scores to between 0 and 8. In contrast, normal sera giving scores of 21–29 were considered non-inhibiting. Sera obtained from venous blood samples always gave clear-cut reactions, whereas intermediate reactions (score 10–15) were met with in 4 of the samples of capillary blood from children in a family material.

The specificity of the agglutinating substance in serum J.K. was ascertained by the following observations:

1. The investigation of sera from 119 unrelated individuals (including the parents in the family material) gave the following result:

	Inhibition of agglutination	No inhibition of agglutination
Gm(a+) 73	51	22
Gm(a−) 46	46	0

The probability that the hæmagglutinating substance in serum J.K. is unrelated to the Gm system is $p < 0{\cdot}0001$ ($\chi^2 = 16{\cdot}99$ for 1 degree of freedom).

Among the 73 Gm(a+) individuals, 56 were probably heterozygous (*Gm*^{a}/*Gm*) and 17 homozygous (*Gm*^{a}/*Gm*^{a}), as calculated from the gene frequencies. Actually, 51 of the sera inhibited the agglutinating substance in serum J.K., while 22 sera did not. The difference between the observed and expected values is not significant ($\chi^2 = 1{\cdot}92$ for 1 degree of freedom).

2. Sera from the members of 25 families with 66 children were studied.

Among the children, 26 were of type Gm(a−). Sera from 25 of them inhibited the agglutinating substance in serum J.K., while one serum showed an intermediate reaction. If one assumes that the serum giving an intermediate reaction really is inhibiting, the probability that this distribution is merely due to chance is $P = 0{\cdot}025$ (Fisher's exact method).

Based on Gm^a type determinations, the genotype *Gm*^{a}/*Gm* could be proved in 24 individuals. Of these sera, 22 inhibited the agglutinating substance in serum J.K., while 2 showed intermediate reactions. If again the assumption is made that the two sera really are inhibiting, the probability that this distribution is due to chance is $P = 0{\cdot}043$ (Fisher's exact method).

When all children (4 or more) in matings of type Gm(a+) × Gm(a−) were Gm(a+), the Gm(a+) parent was expected to be of genotype *Gm*^{a}/*Gm*^{a}. Similarly, when 4 or more Gm(a+) children were found in a mating of type Gm(a+) × Gm(a+), one of them was expected to be of genotype *Gm*^{a}/*Gm*^{a}.

On this basis, 6 individuals in the family material were expected to be of genotype *Gm^a/Gm^a*. Sera from 5 of them did not inhibit the agglutinating substance in serum J.K., while one serum did so. The probability that this is merely due to chance is $P = 0{\cdot}05$ (Fisher's exact method).

In seven families, one or more children were thought to be of genotype *Gm^a/Gm^a* because their sera did not inhibit the agglutinating substance in serum J.K. In all these matings, both parents were of type Gm(a+). The probability that this is due only to chance is $P = 0{\cdot}00091$.

The fourth intermediate reaction was observed in a child of type Gm(a+), whose genotype could not be predicted.

From these observations, it is concluded that the agglutinating substance in serum J.K. reveals the substance determined by the gene *Gm*. The serum is therefore called anti-Gm in accordance with previous designations[2] of sera related to the Gm system. The term anti-Gm does not imply that the agglutinating substance is necessarily the result of previous immunization; it is simply a designation based on the observation that the agglutinating substance in serum J.K. reacts with the Gm substance.

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Exploratory Physicochemical Studies on the Sense of Taste

IN the past, many chemists have tried to account for the tastes of substances in terms of their chemical structures. Although limited correlations have been found, no rigid, widely applicable generalization has evolved. In view of the poor success in this direction, it is apparent that the relationship is very complex. With the belief that taste, as well as other physiological responses, will be understood eventually in terms of the molecular properties of substances, a deliberate search was begun in this laboratory to identify these properties for the sense of taste.

Our general plan of attack has been twofold[1]. One approach is to postulate a mechanism by which the sapid substance can trigger a nerve impulse to the brain to be recognized as a taste sensation and then to examine the molecular properties related to this mechanism. The second approach is to search for correlations between taste and molecular properties with the hope that one or more will be found to give a clue to the mechanism of taste stimulation. Space does not permit an elaboration of the reasoning followed in choosing the properties to be measured. Furthermore, since no positive generalizations have been discovered, it is sufficient to report only the experimental results.

A specific group of compounds was selected the tastes of which range from tasteless to 4,000 times as sweet as sucrose. The relative sweetnesses were determined by a taste panel under the supervision of Drs. Frank Pilgrim and Howard Schutz of the Quartermaster Food and Container Institute, U.S. Army, Chicago. Several isomeric pairs were chosen, including optical isomers, in order to have a critical test for any relationships discovered. Attention was confined to the sweet taste in order to keep the number of variables to a minimum and because structural modifications can be made to elicit a wide variation in intensity of response.

Table 1. COMPOUNDS STUDIED AND THEIR PROPERTIES

Compound	Relative sweetness		$E_{1/2}$[a] (volts)		Wet-melting point depression[b] (° C.)	Surface[c] tension at $10^{-4}M$ (dynes/cm.)
	This study	Lit.[d]	This study	Lit.[d]		
Sucrose	1·00	1·00	−0·85*			62·0
Fructose	1·15	1·73 1·05	−1·86	−1·80		60·8
α-D-Glucose	0·64	0·74 0·35	−1·56	−1·58	78	55·4
Galactose	0·59	0·32	−1·55	−1·57		
Mannose	0·59		−1·53			
Lactose	0·33	0·16				
Sucrose octaacetate	bitter		−1·05*			
Glucose penta-acetate	bitter		−1·02*			
α-Methyl glucoside	0·52		none			
Stevioside	280	*c.* 300				53·7
Saccharine	306	425–675 450–500	−1·73†	−1·94 (*p*H 10) −1·25 (*p*H 2)		
Dulcin	91					
Sucaryl	33·8	*c.* 30				
2-CH_3O-5-NO_2-aniline	167	220–330 2,150	−0·43†		10	57·5
4-CH_3O-3-NO_2-aniline	tasteless		−0·42†		9	54·0
2-C_2H_5O-5-NO_2-aniline	703	950–1,400 830	−0·48†			
4-C_2H_5O-3-NO_2-aniline	tasteless					
2-*n*-C_3H_7O-5-NO_2-aniline		4,100 3,100				
2-HO-5-NO_2-aniline	20·5	120–200	−0·48†		60	
4-HO-3-NO_2-aniline	not sweet		−0·31		20	
2-CH_3-5-NO_2-aniline	298	sweet	−0·40†			
4-CH_3-3-NO_2-aniline	not sweet		−0·42†			
2-CO_2H-5-NO_2-aniline	not sweet		−0·34			
2-Cl-5-NO_2-aniline	375	400 700	−0·35			7
4-Cl-3-NO_2-aniline	not sweet		−0·40			9
2-Br-5-NO_2-aniline	714	800 1,750	−0·33		10	63·7
4-Br-3-NO_2-aniline	not sweet		−0·34		11	66·9
m-Nitroaniline		40	−0·38	−0·43		
Nitrobenzene			−0·42	−0·48 (*p*H 5·7)		
D-Tryptophan	222	sweet				
DL-Tryptophan	111	sweet				
L-Tryptophan	not sweet	not sweet				
D-Asparagine	2·1	sweet				
L-Asparagine	not sweet	not sweet				

[a] $E_{1/2}$, the half-wave reduction potential with reference to the saturated calomel electrode, measured with a Sargent–Heyrovsky model XII recording polarograph at 37·1 ± 0·03° C. and *p*H 6·6.

[b] Wet-melting point depression, namely, the difference between the melting point of a substance when dry and when in contact with water, and is used as a measure of the degree of association of the substance with water.

[c] Measurements made by Mr. Andrew Wims.

[d] Literature sources of data cited in Table 1 may be obtained from the authors.

* Conceivably the value for an impurity; however, every precaution was taken to use materials of highest purity. The same value was obtained, for example, using sucrose of grade National Bureau of Standards Calorimetry Standard, m.p. 171–174° C., and Fisher Scientific Certified Reagent, m.p. 182–184° C.

† Gelatine added as a suppressor.

Table 2. ADSORPTION CHARACTERISTICS OF SWEET AND TASTELESS ISOMERIC NITROANILINES

Compound	Wave-length for analysis	Molar absorbancy index
	(mμ)	
(I) 2-Bromo-5-nitroaniline (sweet)	247	9,840
(II) 4-Bromo-3-nitroaniline (tasteless)	237	16,320
(III) 2-Methoxy-5-nitroaniline (sweet)	253	12,320
(IV) 4-Methoxy-3-nitroaniline (tasteless)	228	16,900

Compound	Adsorption on charcoal			Adsorption on hair		
	α	$1/n$	W	α	$1/n$	W
I	0·340	0·830	0·0743	0·0436	0·417	0·0095
II	0·248	0·671	0·0538	0·0495	0·484	0·0108
III	0·269	0·732	0·0585	0·0244	0·494	0·0041
IV	0·186	0·745	0·0403	0·0125	0·275	0·0021

In the search for correlations between taste and molecular properties, a few properties which could affect the taste of a compound were studied first. Although some of these properties had been measured by previous investigators, the present work differs in that all measurements were made by the same group of investigators on compounds the tastes of which had been evaluated by the same panel. The results are given in Table 1.

Our second approach for finding a clue to the molecular properties responsible for characteristic tastes is to consider mechanisms by which sapid substances might trigger nerve impulses to the brain. Table 2 contains the results of a search for a correlation between the sweet taste and adsorption on a certain surface. Charcoal was used first in order to work out the experimental procedure. The hair was that of a child, washed in a nonionic detergent, and air-dried at room temperature. Two types of tongue tissue were used in unreported experiments but the results were not reproducible. The results in Table 2 fit the Freundlich equation :

$$x = \alpha c^{1/n}$$

where x represents millimoles of adsorbate held per unit weight of adsorbent ; c the concentration of adsorbate remaining unadsorbed at equilibrium in moles/litre ; α and n are constants ; while, in Table 2, W is the weight of substance adsorbed at the concentration of 0·01 gm./100 gm. solution.

Experiments were done to detect any special interaction between sweet compounds and certain biological substances. The results from one type of experiment are given in Table 3, from which no significant difference is observed between a sweet compound and its tasteless isomer. The numbers I and II refer to the compounds in Table 2. Other experiments were conducted to learn whether or not certain components common to enzyme systems are involved in taste chemireception. Thus, sweet solutions of 2-methoxy-5-nitroaniline and salty sodium chloride solutions were tasted in a helium atmosphere. Other than a sort of warming sensation, no significant difference in taste from that in air was observed. Sweet solutions of 2-methoxy-5-nitroaniline were tasted when diluted with solutions of magnesium chloride, manganous chloride, or water. The solutions containing magnesium or manganous ions were bitter and sweet, and magnesium ion could not be distinguished from manganous ion by taste. Then, to see whether or not the sapid substance interacts directly with an enzyme, solutions of a sweet compound were tasted in the presence of certain enzyme inhibitors. For example, several aliquots of a sweet solution of 2-methoxy-5-nitroaniline were diluted separately with water, or with solutions of sodium azide, potassium fluoride, sodium iodoacetate, or sodium cyanide. These solutions were mixed and tasted in random order several times without their identity being known to the taster (L. N. F.). Azide enhanced the sweetness of the nitroaniline, but fluoride and iodoacetate diminished the sweetness a very small amount, iodoacetate gave an iodine flavour, and cyanide was very bitter, outweighing the sweet taste. However, none of these recognized enzyme inhibitors obliterated the sweet taste irreversibly. This fact suggests that the taste receptor surface is not that of an enzyme.

Thus several physical properties which conceivably could be factors determining the tastes of substances have been measured. Also, various possible mechanisms for stimulus-receptor interactions have been examined. Although no positive generalizations have been found, and these experiments have been exploratory, the results serve as guides for future work in pursuing the identity of the molecular proper-

Table 3. LIGHT ABSORBANCIES OF VARIOUS SOLUTIONS ALONE AND WHEN MIXED

Compound	A^a	Sum	Change when mixed (per cent)	Compound	A^b	Sum	Change when mixed (per cent)
I	0·438			II	0·182		
Saliva	0·444	0·882		Saliva	0·200	0·382	
Mixture	0·845		−4·2	Mixture	0·360		−5·75
I	0·438			II	0·428		
Bovine gamma globulin	0·064	0·502		Bovine gamma globulin	0·135	0·563	
Mixture	0·486		−3·2	Mixture	0·534		−5·5
I	0·428			II	0·418		
ATP	0·145	0·573		ATP	0·078	0·496	
Mixture	0·563		−1·8	Mixture	0·478		−3·6
I	0·408			II	0·398		
ATP	0·112			ATP	0·048	0·446	
Mg^{2+}	0·000	0·520		II, ATP, Mg^{2+}	0·452		
Mixture	0·528		c. 0	II, ATP	0·452		c. 0
I	0·433			II	0·423		
Globin*	0·051	0·484		Globin	0·053	0·476	
Mixture	0·449		−7·8	Mixture	0·452		−5·3
Mixture + Mg^{2+}	0·452			Mixture + Mg^{2+}	0·454		

[a] Measurements made at the $\lambda_{max.}$ of I.
[b] Measurements made at the $\lambda_{max.}$ of II.
* A filtered colloidal solution of globin.
ATP, adenosine triphosphate.

ties responsible for the characteristic tastes of substances. It is to be realized that the nature of the stimulus-receptor interaction is unknown and these exploratory-type experiments constitute an attempt to find a clue on a gross level.

This work was undertaken in co-operation with the Quartermaster Food and Container Institute for the Armed Forces, Quartermaster Research and Engineering Command, U.S. Army.

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Energy Compensation in the Crabtree Effect with Ehrlich Ascites Carcinoma Cells

RECENTLY, Quastel and Bickis[1] published a very interesting and stimulating article concerning the energy relationships in several intact cell types, including the Ehrlich ascites carcinoma cell. They determined the ratio of lactate produced to the difference between oxygen consumed in the cell system with and without added glucose (average value 5·8). The assumption was made that the amount of adenosine triphosphate produced in the two systems was the same. They reasoned that if the total production of energy remained constant in the two cell systems, the ratio phosphorus/oxygen would be about 3.

Table 1. ENERGY RELATIONSHIP BETWEEN GLYCOLYSIS AND THE DEPRESSION OF RESPIRATION OF THE CRABTREE EFFECT

Compound (μM per ml. cells)	With glucose	Endogenous	$\frac{\text{Lactate}}{\Delta\ \text{Oxygen}}$
Oxygen utilized	16·3	27·7	
Lactate accumulated	57·2	—	5·0
Adenosine triphosphate present	1·60	1·65	(P : O = 2·5)

Incubation system: 12·4 volume per cent of tumour cells in phosphate Locke's solution, pH 7·4; 30° C. for 15 min.; glucose 51·7 μM per ml. cells.

We recently published observations[2] on the Ehrlich ascites cells which show that the adenosine triphosphate content of the endogenous- and the glucose-containing cell is the same, except for an initial brief period of equilibration. This means that glycolysis does produce an amount of energy equivalent to the energy lost by the decreased oxygen consumption, provided the utilization of adenosine triphosphate remains constant. Furthermore, Table 1 shows that the accumulation of lactate could nearly account for the decrease in oxygen consumption in terms of production of adenosine triphosphate, assuming a phosphorus/oxygen ratio of approximately 3 (2·5) and glycolytic production of 2 molecules of adenosine triphosphate per glucose molecules. These results are in good agreement with Quastel and Bickis's hypothesis.

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PATHOLOGY

Homologous Species Neoplastic Antibodies

Prehn and Main[1], in a review of the subject, state that the demonstration of circulating cytotoxins is much simpler when heterologous tissue transplants are used as antigens than when homologous tissues are used. Schrek and Preston[2], using the Bagg rat lymphosarcoma in Sprague–Dawley rats, report the successful demonstration of serum cytotoxins in the rats (25 per cent of the total) in which the tumour had regressed.

The present communication deals with a limited investigation on the response of a human male to two cultures of human adenocarcinoma, arising in two different individuals.

Cultures of the neoplastic tissue were used instead of tissue homogenates in an effort to obtain as pure a cellular antigen as possible. Fresh cultures were used instead of known cultures of long standing because of the reported tendencies of long-term culture lines to become alike in antigenic characteristics[3].

(1) A healthy white male, blood type O,Rh-positive, was used as the antibody producer.

(2) Fragments of three adenocarcinomas were obtained from males at primary surgical removal and cultured by Puck's methods until pure cultures of the neoplastic cells were obtained. These separate cultures were labelled *C.P.*, *A.N.* and *C.G.*

(3) A portion of the living culture *C.P.*, estimated to be of the order of 10,000,000 cells, was suspended in salt solution and injected subcutaneously in the upper arm. The implant increased in size for ten days with marked local redness of the skin and moderate tenderness. By the fourteenth day the implant had decreased in size by 50 per cent. There was no systemic effect noted.

On the eighteenth day a similar amount of culture *C.P.* was introduced as before in a new location. The local reaction was immediate but decreased by half by the sixth day after implantation.

A third implantation of like amount was accompanied by local reaction more violent than the preceding two and by mild general systemic reaction lasting 24 hr. Disappearance of the local mass was almost complete at the end of the sixth day.

Seven days after the third implantation of *C.P.*-cultured cells, blood was withdrawn, the serum separated and an amount of this serum, equal to 1/400 of the total nutrient solution, was added to the nutrient solution consisting of 40 per cent adjunct nutrient solution. The nutrient solution, minus the immune serum addition, was the one used previously on all cell cultures and had proved adequate for growth.

A culture each of *C.P.*, *A.N.* and *C.G.* was drained of nutrient solution, washed and the nutrient solution containing the immune serum introduced.

The cultures were examined at 6, 12 and 24 hr. Culture *C.P.* at the end of 6 hr. showed nuclear degeneration, the nucleus in most cases forming an amorphous halo. There was marked rounding and shrinking of the cells. Subcultures taken at this time failed to grow, as did those made at 12 and 24 hr. Cultures *A.N.* and *C.G.* showed no effect of the immune serum, and both were successfully subcultured.

An identical series of implantations on the same individual were made except that in the second case cultures of *A.N.* were used as antigen. There were no major differences in reaction as compared to the first run.

The immune serum, used in the same concentration as before, now produced nuclear degeneration and death of cells in both culture *C.P.* and *A.N.* Culture *C.G.* remained unaffected by the immune serum–nutrient mixture, both morphologically and by successful subculture.

Heating the immune serum for 40 min. at 56° C. destroyed its cytotoxic activity, which was restored on the addition of fresh non-immune human serum.

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PSYCHOLOGY

The Water–Salt Receptor and Preference in the Rat

Zotterman[1] and his co-workers have reported that in the rat and in man the taste of water consists in a reduction of the spontaneous firing of the salt receptors. According to Deutsch's theory[2] of need and reward, satiation of thirst is due to the reception of a certain quantity of messages signalling the ingestion of water. The quantity of fluid ingested would be proportionate to the number of signals generated by it. It follows that as a hypotonic solution of saline reduces the spontaneous firing of salt receptors less than the same volume of water, it would generate less of a 'water signal'. A rat should therefore drink more saline solution even when water is present. This has already been noted by workers such as Richter[3] and Bare[4] and ascribed to a preference for weak saline solutions. But if the above hypothesis is correct, the ingestion of saline by the rat is not due to a preference but to the fact that it has been given 'diluted water', if we can put it that way.

On this theory a certain amount of reward is also proportionate to the total quantity of messages signalling the ingestion of a goal substance. Therefore if this hypothesis is correct, we should predict the opposite 'preference' in a situation where the intake of each fluid is restricted to a certain volume. Thus rats, when they are forced to choose between equal amount of water and saline in a maze, should learn to run to the water arm, as a given volume of saline generates fewer signals than the same volume of water. Accordingly, two experiments were carried out.

The first was carried out in a T-maze. Nine rats, aged 4 months, were given 2 hr. of *ad lib.* water drinking a day and *ad lib.* food except during maze running. Each animal was given 15 runs a day in the T-maze under 20 hr. of water deprivation to rewards of water in one arm and 0·5 per cent saline in the other, four animals receiving water in the right arm and five in the left. The average number of runs to water over the 6 days was 56, and to the saline, 34 (significant at the 0·001 level of probability).

In the second experiment, a group of 10 rats was put on the same schedule as those above. They were presented with two water bottles for half an hour when they were 20 hr. thirsty, one containing 0·5 per cent saline, the other water. The position of the bottles varied. The experiment confirmed that during eight days the average amount of saline drunk was 59 c.c. as against 36 c.c. (significant at the 0·01 level of probability).

The experiment therefore confirms the prediction and also casts considerable doubt on the conventional ways of measuring preference. It is hoped to investigate further the behaviour of species which lack this gustatory arrangement, and other parameters of the ingestion of saline by the rat. Further, the spontaneous rate of firing of the saline receptors should vary with the degree of salt depletion. This should in its turn reduce the level of water intake. Whether such a simple control mechanism does in fact govern the ingestion of water in relation to salt suggests a further line of investigation.

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PALÆONTOLOGY

Precambrian Coelenterata from Australia, Africa and England

Extensive collecting has been carried out during the past two years by private collectors, the South Australian Museum, the University of Adelaide and Mr. R. C. Sprigg and associates, in flaggy quartzites near the base of the Cambrian at the old Ediacara mines, 280 miles due north of Adelaide, South Australia. Sprigg[1] found and described as jellyfishes fossil remains of soft-bodied animals from this locality. The study of the abundant new material[2], which comprises about 800 specimens, has led to the following results. (1) The fauna consists not only of the forms described by Sprigg as scyphozoan and hydrozoan medusæ, but also of Anthozoa representing the Octocorallia, of Annelida[3], and of at least two entirely new types of soft-bodied invertebrates[2,3]. (2) Certainly one and possibly more elements of this fauna belong to genera described from the Kuibis Quartzite of the Nama System in South Africa, and one genus recently described[4] from the Precambrian of Charnwood Forest, Leicestershire, also occurs at Ediacara. (3) New stratigraphical and palæontological evidence indicates Late Precambrian age of the Ediacara fauna.

The most striking and unexpected discovery is the common occurrence of representatives of the South African genus *Rangea* Gürich[5] in the Ediacara fauna. About forty specimens are now known, and one new species has been described, though further finds may indicate the presence of more species in this material. It is preserved in different forms, which can be interpreted as different aspects and stages of preservation of the soft body. Some specimens show a long stalk attached to the leaf-shaped main body. This has either a median field or a median zig-zag furrow, and lateral furrows branching out from it. A spicular structure is seen occasionally in the body and stalk. The details of these structures, which will be described elsewhere[2], clearly establish a close relationship between *Rangea* and the living Pennatulacea. In.

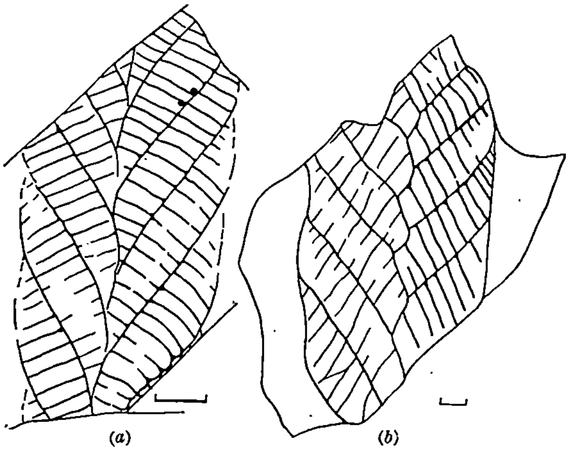

Fig. 1. *a*, Portion of the 'frond' of *Charnia masoni* Ford from the Precambrian of Charnwood Forest, Leicestershire (copy of portion of Ford's Pl. 13, Fig. 3). *b*, *Charnia* sp. from Ediacara, South Australia. S. Aust. Mus. No. P12897. Length of each scale 1 cm.

this order of the Anthozoa the polyps sit either on the rhachis or on discrete leaf-like lateral extensions; *Rangea* may be intermediate between these two groups as the lateral 'branches' are not free as in *Pennatula* but form a single leaf. The genus *Pteridinium* Gürich, which is common in the Kuibis Quartzite, is at present represented in the South Australian fauna only by two poorly preserved specimens. As Richter has observed, it belongs to the same family as *Rangea*; but this cannot be placed in the Gorgonacea with which it has no distinctive features in common, but belongs to the Pennatulacea. These had been previously reported from the Tertiary, Cretaceous and Jurassic and, with some doubt, from the Silurian and Ordovician.

The recent discovery[4] of fossils in the Charnian of Charnwood Forest is of extraordinary interest in this connexion. A single specimen from Ediacara, with the proximal and distal ends broken off (Fig. 1), was classified as *Rangea*(?) sp. before the description of *Charnia* Ford became available. There is no doubt that the two fossils are congeneric; but the South Australian specimen is almost twice the size of the holotype of *Charnia masoni* Ford. The author left the affinities of this fossil in doubt but concluded that it "may most rationally be interpreted as an algal frond. . . . The only likely alternative is that they [that is, *Charnia* and the associated *Charniodiscus*] represent a primitive coelenterate of unknown affinities". *Charnia* is sufficiently close to *Rangea* to be considered as related to the Pennatulacea.

This raises the question of the nature of *Charniodiscus*. Ford has suggested a possible relationship with *Charnia*, with the medusoid disk-like fossil forming the base of the stalk to which the frond-like *Charnia* is attached at the other end. A similar relationship between some of the medusoid fossils from Ediacara from which stalk-like bands emerge and the stalked *Rangea* has been considered, but the two have not yet been found actually joined in one specimen. The presence of a disk-shaped base would distinguish *Rangea* and *Charnia* from all living Pennatulacea in which the end of the stalk is merely club-shaped; but in my opinion it would not exclude close relationship. The presence of a medusa-like base which would correspond to the primary axial polyp of a Pennatulacean could lead to phylogenetic speculations about the still obscure relationships of Scyphozoa and Anthozoa. Such speculation would be premature; but it should be kept in mind when the medusoid Precambrian fossils are re-examined.

The Ediacara fauna is placed in the Late Precambrian for the following reasons.[3] It is found 100–200 ft. below the top of a widespread thick quartzite formation (Pound Quartzite) which is conformably overlain by about 500 ft. of limestones with *Archaeocyatha* and brachiopods in the uppermost beds. This assemblage No. 2 of Daily[6] is widespread in South Australia and can be confidently placed low in the Lower Cambrian. Boulders of Archæocyatha limestones with this and successive assemblages Nos. 3 and 4 occur below shales with Late Lower Cambrian protolenids and *Redlichia* on Kangaroo Island. The Ediacara fauna, taken from a horizon below an early Lower Cambrian fauna, is unlike any known Cambrian fossil assemblage. It is therefore correctly assigned to the Late Precambrian. The same age can now be suggested on palæontological grounds for the Kuibis Quartzite of the Nama Group and for the fossiliferous strata of the Charnian.

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CHEMISTRY

Some Alkyl-Aryl Sodium Sulphonates as Standard Substances in Detergent Chemistry

In the course of work on the behaviour of commercial detergents of the anionic type, we needed some standard substances with which to compare the commercial products. The sodium sulphonates of the straight-chain substituted benzene hydrocarbons appeared to be likely compounds. The required hydrocarbons from butyl benzene to tetradecyl benzene were synthesized from the fatty acids with even numbers of carbon atoms. The branched-chain compound α-dimethyldecyl benzene was also synthesized. From the hydrocarbons the sodium sulphonates were prepared and purified. The behaviour of these compounds in solution was studied by means of the methylene blue method of Longwell and Maniece[1] and by paper chromatography.

Methylene blue tests on pure sodium sulphonates of the hydrocarbons. Standard solutions of the pure sodium sulphonates of the hydrocarbons were prepared by weighing known amounts of the pure dry substances and dissolving in water to standard volumes. There is a decrease in solubility with increasing chain-length, and special care is required to obtain solutions of the higher members at a suitable concentration. As an example, the solubility of sodium-tetradecylbenzenesulphonate is 6·5 parts per million at 20° C. Aliquots of these solutions were examined by the methylene blue method, and the optical densities of the resulting coloured chloroform extracts were recorded. After allowing for reagent blanks, which were run with each experiment, plots were made of optical density against concentration and from the graphs so obtained Table 1 was derived. From column 4 of Table 1 it is seen that optical

Table 1

Substance	Molecular weight	Value of optical density 200 μgm. of sulphonate	Optical density × molecular weight	
n-Tetradecylbenzene-sulphonate	376	0·935	352	Average value 347
n-Dodecylbenzene-sulphonate	348	1·010	351	
n-Decylbenzene-sulphonate	320	1·075	344	
n-Octylbenzene-sulphonate	292	1·166	340	
n-Hexylbenzene-sulphonate	264	1·138	300	86% of av.
n-Butylbenzene-sulphonate	236	0·106	22	6% ,,
α-Dimethyldecyl-benzenesulphonate	346	0·926	320	93% ,,
Alkylbenzenesulphonate of commerce	356	0·926	330	96% ,,
'Manoxol O.T.'	444	0·780	346	100% ,,

density multiplied by the molecular weight is approximately a constant for the members of the series from *n*-octylbenzene upwards. This is a useful check on the molecular weight of an unknown compound of similar composition. Figures for α-dimethyldecylbenzene sodium sulphonate, the alkylbenzene sodium sulphonate of commerce and for manoxol (sodium-dioctylsulphosuccinate) are included for purposes of comparison. The sodium sulphonates below butyl benzene in the series give no colour under the conditions of the Longwell–Maniece test.

Paper chromatography of some alkyl-aryl sodium sulphonates. Commercial detergents of the alkyl-aryl sulphonate type are difficult to study by paper chromatography, and special methods such as that of F. Franks[2] have been devised for their examination. The difficulties appear to be due to their detergent properties which cause them to remove other substances, including other detergents, from the paper and to carry them forward with their own movement. These remarks also apply to α-dimethyldecylbenzene-sodium sulphonate and to detergents of the 'Teepol' type. With the straight-chain alkyl-aryl sulphonates there are no such effects and chromatography proceeds normally. Values of R_F for four such compounds in various mixtures of alcohol and water are given in Table 2. Whatman No. 4 paper was used and the spots were shown up with a solution of rhodamine 6*B* used as a spray at a concentration of 0·05 per cent w/v.

Table 2. R_F VALUES

Substance	Per cent alcohol/water by volume					
	10	30	35	40	50	100
n-Octylbenzene-sulphonate	0·67	0·81	0·82	0·83	0·87	0·89
n-Decylbenzene-sulphonate	0·03	0·54	0·74	0·75	0·84	0·89
n-Dodecylbenzene-sulphonate	Nil	0·22	0·23	0·23	0·76	0·89
n-Tetradecylbenzene-sulphonate	Nil	0·06	0·06	0·10	0·20	0·89

We wish to thank the Government Chemist for permission to publish this communication.

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Labelling of Radiographic Contrast Media with Iodine-131

THE rapid development and general acceptance of contrast media represents one of the outstanding successes of diagnostic röntgenology. Roentgen contrast media are generally di- or tri-iodo derivatives of benzene or pyridine, containing further substituents influencing solubility. The most widely used contrast compounds are 3,5-diiodo-4-pyridon-N-acetic acid as its diethanolamine salt ('Iodopyracet', 'Diodrast', 'Diodone', 'Ioduron', etc.), and N-methyl-3,5-diiodo-chelidamate as its disodium salt ('Neo-Iopax', 'Iodoxyl', 'Uropac', etc.). A new compound of the urotropic class is sodium-3-acetyl-amino-2,4,6-tri-iodobenzoate known as 'Triopac', 'Urokon', 'Triumbren' and diacetylamino-2,4,6-triiodobenzoic acid, the methylglucamate of which is known as 'Urografin'. The hepatotropic contrast media are represented by N,N′-adipyl-*bis*(3-amino-2,4,6-triiodo)-benzoic acid as methylglucamate ('Biligrafin' or 'Cholografin') and 2-ethyl-3-(3′-amino-2,4,6-triiodophenyl)-propionic acid ('Cistobil', 'Telepaque').

The application of these contrast media for diagnostic purposes gives only a static picture. Pathological changes are diagnosed on the basis of permanent differences in the morphological picture. It is not generally possible to gain information on the functional state of the organs by these means.

The labelling of contrast compounds with iodine-131 opens the possibility of investigating the functional state of the organs by measuring the amount of the compound applied and excreted and its concentration. Indicator diagnosis with the aid of labelled contrast media allows the registration and analysis of the dynamics of processes, and therefore combines both possibilities.

In this communication a method for labelling the more important contrast media with iodine-131 is presented; these are 3,5-diiodo-4-pyridon-N-acetic acid ('Ioduron', 'Diodon'), 3-acetylamino-2,4,6-tri-iodobenzoic acid ('Triopac', 'Triumbren'), N,N′-adipyl-*bis*(3-amino-2,4,6-triiodo)-benzoic acid ('Biligrafin') and 3,5-diacetylamino-2,4,6-triiodobenzoic acid ('Urografin'). An exchange reaction method was used. The use of labelled contrast media ('Triopac') for determining the vitality of bone tissue will be described elsewhere.

Sodium-3-acetylamino-2,4,6-triiodobenzoate-^{131}I, the preparation used, was 'Triopac-400' (Cilag A.G., Schaffhausen, Switzerland) or 'Triumbren' (Spofa, Prague); 2 ml. of the solution contains 1·292 gm. of the sodium salt.

To 2 ml. of 'Triopac-400' solution were added 8 ml. acetate buffer solution *p*H 5, 1 ml. potassium iodide carrier solution (20 mgm. in 100 ml. water) and 4 ml. potassium iodide-131 solution with a radioactivity of 9 mc. The mixture was heated under reflux on the water-bath for 12 hr. The solution was then allowed to cool to room temperature and free 3-acetylamino-2,4,6-triiodobenzoic acid precipitated by addition of concentrated phosphoric acid to *p*H 1. The precipitate was filtered by suction and washed with cold water until the volume of the filtrate was exactly 32 ml. The loss of radioactivity amounted to 1·5 per cent. The precipitate was dissolved in a slight excess of ammonia and the precipitation repeated twice (yield, 1·12 gm. of the free acid (89 per cent) and 90 per cent of the original radioactivity). The purity of the 3-acetylamino-

2,4,6-triiodobenzoic acid was controlled by chromatography in butanol/ammonia/water (50 : 5 : 45) on Whatman No. 3 paper. The acid was detected by radioactivity measurement, and the potassium iodide by oxidation to iodine with 0·1 N ferrous nitrate solution containing 3 per cent of hydrogen peroxide and starch. The recrystallized products were not contaminated by potassium iodide.

3,5-Diacetylamino-2,4,6-triiodobenzoic acid-^{131}I, 'Urografin' solution 76 per cent (Schering A.G., Berlin), containing 2 gm. of the sodium and 13·2 gm of the methyl-glucamine salt in 20 ml. (2 ml. of the 'Urografin' solution correspond to 1·193 gm. of 3,5-diacetylamino-2,4,6-triiodobenzoic acid) were iodinated by the exchange reaction described above. The yield was 0·775 gm. (65 per cent) of the acid and 66·4 per cent of the original radioactivity. The product was chromatographically pure.

3,5-Diiodo-4-pyridon-N-acetic acid-^{131}I, 70 per cent 'Ioduron' (Cilag A.G.) or 'Diodon' (Spofa) was employed as the diethanolamine salt. 2 ml. 70 per cent 'Ioduron', corresponding to 1·11 gm. of the free acid, was labelled as described above. The yield was 67 per cent of the acid and 70 per cent of the original radioactivity. The product was chromatographically pure.

5 ml. of a 30 per cent solution of the methylglucamine salt of 3,3′-(adipyl-diimino)*bis*-2,4,5-triiodobenzoic acid 'Biligrafin' (Schering A.G., Berlin) containing 1·125 gm. of the free acid was labelled as above. The yield was 45 per cent of the acid and 46·5 per cent of the original radioactivity. The product was chromatographically pure. Identical yields were obtained with the corresponding Spofa product.

The radioactivity of the samples was determined in liquid samples with the aid of a scintillation counter.

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Infra-red and the Near Ultra-violet Absorption Spectra of Polyphenyl Derivatives of the Elements of Groups IV*b* and V*b*

We have been investigating the infra-red and the near ultra-violet absorption spectra of several polyphenyl derivatives of the elements of groups IV*b* and V*b*. In the case of the derivatives of the V*b* elements, we have studied the spectra of derivatives where the central atoms possess and do not possess unshared *p*-electrons (derivatives of the atoms in their 'trivalent' and 'pentavalent' states respectively). In addition, we have been studying the spectra of *o*-, *m*- and *p*-substituted tritylbenzenes (trityl = triphenylmethyl). The ultra-violet spectra were recorded in alcohol solutions, and the infra-red spectra in mulls and also in solutions.

Our results on the ultra-violet spectra of the triphenyl derivatives of the V*b* elements ($M\,Ph_3$ where M = V*b* element) agree well with those of Jaffe[1] and show trends similar to the derivatives of the type $Ph\,M\,Me_2$ studied by Bowden and Braude[2]. The ultra-violet spectra of the triphenyl and tetraphenyl halides ($Ph_n M\,X_m$ where X = Cl or Br and $n + m = 5$) are similar to those of the other derivatives of the pentavalent atoms[1–4]. In general, the phenyl derivatives of the V*b* elements in the trivalent state exhibit only one strong absorption band ($n \rightarrow \pi^*$) while the pentavalent atom compounds show vibrational structure ($\pi \rightarrow \pi^*$) similar to the secondary band (B-band at 2500 A.) of benzene itself. This indicates that the unshared *p*-electrons in the trivalent atom derivatives participate in resonance interaction with the π-electrons of the benzene system. This is further demonstrated by the progressive bathochromic shifts observed with the increase in the number of phenyl groups on the central atom. Such variations in spectra are considered to be proportional to the magnitude of the resonance interaction of the phenyl groups with the central atom[5]. The positions of the secondary bands of aniline, diphenylamine and triphenylamine are found to be 2800, 2850 and 2970 A. respectively. The primary band (E-band) seems to vary little, having the values of 2300 and 2280 A. for aniline and triphenylamine. Jaffe[1] did not seem to observe such variations in the secondary bands in the series PhNMe_2, Ph_2NMe and NPh_3 because of the bathochromic shifts due to the methyl groups. He, however, obtained a progressive increase in the primary band wave-length with the number of the methyl groups. It is interesting to see that in spite of the bathochromic shift caused by the methyl groups, P Ph_3 absorbs around 2610 A. compared with 2510 A. in the case of Ph P Me_2. The intensity is also considerably greater in the former compound. The arsenic and antimony derivatives also show similar variations.

Among the $M\,Ph_3$ derivatives of the V*b* elements, N Ph_3 shows the largest hyperchromic effect, which seems reasonable, nitrogen being a first-row element. There is a marked decrease in the wave-length and the intensity in the case of P Ph_3 and a further decrease in the wave-length in As Ph_3. While in phosphorus the 3*d* shell is vacant, in arsenic it is completely filled. But while going from As Ph_3 to Sb Ph_3 and Bi Ph_3 there are progressive shifts to longer wave-lengths (2480, 2560 and 2800 A.). This is considered to be due to the predominating influence of the decreasing ionization potential of the central atom. The importance of the ionization potentials in determining such bathochromic shifts has been recognized[6,7]. Bi Ph_3 also shows another shoulder around 2500 A., which may represent dissociation.

The presence of the vibrational structure of benzene in the derivatives of the pentavalent V*b* atoms indicates negligible or no resonance interaction of the central atoms with the π-electrons of the benzene system. The spectra of these derivatives show little variation with the number of phenyl groups attached to the atom. For example, both tetraphenylstiboniumchloride and triphenylstiboniumdichloride show the absorption maxima at 2700, 2630, 2580 and 2530 A. The derivatives of IV*b* elements behave similarly and show almost no variation in their spectra with the number of phenyl groups. Our results on the phenyl derivatives of IV*b* elements agree with those of Milazzo[8] and of Bowden and Braude[2] on derivatives of the type $PhMR_3$ (R = alkyl group). Among IV*b* derivatives, the silicon derivatives seem to show slightly larger bathochromic shifts, while among the V*b* pentavalent atom compounds, the phosphorus derivatives show larger bathochromic shifts. This may possibly be taken as evidence for the expansion of the valence shell in these two second-row elements.

The ultra-violet spectra of the *o*-, *m*- and *p*-substituted tritylbenzenes also show the vibrational structure of benzene. There is little difference between the spectra of the *p*- and the corresponding *m*-derivatives. The *o*-derivatives seem to exhibit considerable steric interaction. Some of the *p*-substituents which have characteristic absorptions in the ultra-violet, exhibit their absorption maxima at the same wave-lengths as they would in the mono-substituted benzenes. There seems to be little doubt that the *p*-trityl group does not interact with the other substituent or with the benzene ring and that the resonance parameter of the trityl group is approximately zero. Further, the overall electronegativities of the *m*- and *p*-trityl groups were both estimated to be about zero, by a study of the characteristic group frequencies of the *m*- and *p*-derivatives in the infra-red. These conclusions are in accordance with the Hammett reactivity constants of the *m*- and *p*-trityl groups, which have been found to be close to zero by Benkeser and Gosnell[9].

All the polyphenyl derivatives of IV*b* and V*b* elements show mass effects (decrease in frequency with increase in mass) in their infra-red spectra. The mass effects are marked in the C═C skeletal vibrations, in some of the frequencies due to the mono-substituted phenyl group and in one of the C—H out-of-plane deformation bands (750 $cm.^{-1}$). The 750 $cm.^{-1}$ C—H out-of-plane deformation bands of these derivatives show unusual splittings. All these derivatives exhibit bands in the regions 1,440–1,400 $cm.^{-1}$ and 1,100–1,000 $cm.^{-1}$, indicating that such frequencies are by no means unique to P *Ph* or Si *Ph* groups[10]. They might as well be due to some activated ring vibrations.

Further work on these systems is in progress and a detailed report will be published elsewhere at a later date. We wish to thank Prof. R. A. Benkeser of Purdue University for kindly providing the pure samples of the tritylbenzenes.

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Binding of Water in Ferric Hydrate

A RECENT communication discussed the infra-red spectra and proton magnetic resonance experiments on some hydroxides and hydrous oxides[1]. We found in the so-called ferric hydrate OH-groups beside free water (adsorbed), that is to say, this compound may be defined as iron(III) hydroxide. In my own communication, the drawing for the infra-red spectrum (Fig. 1) was incorrect; the centre of gravity of curve I should be between $3{\cdot}1$ and $3{\cdot}2\mu$.

In Table 1 herewith, there are the bands of another precipitate with 19·9 per cent water. This was produced from a solution of ferric nitrate with ammonia.

Table 1

Infra-red spectrum of iron(III) hydroxide

Bands in $cm.^{-1}$ (br = broad)	I 3,300 br	II 1,625 br	III 1,030 br
Assignment	OH stretching vibration	H_2O bending vibration	OH bending vibration

From the infra-red spectra of the different iron hydroxides[2], the observed band III is assigned as a bending vibration of the OH-group. The possibility of a combination vibration of the adsorbed water can be excluded. Sometimes this band is split into two. It is possible to calculate[3] the Fe–OH distance with the wave-numbers of the bands I and III as $\sim 1{\cdot}90$ A. This value is of the same order of magnitude as the corresponding distance in the other iron hydroxides (namely, γ-FeOOH, 1·97 A.), and hence the broadening of the bands and the amorphous structure of the compound prejudice the precision of the estimation. The infra-red spectrum of Table 1 may therefore be interpreted as showing that there are OH-groups besides water (adsorbed) in the compound under investigation.

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PHYSICAL SCIENCES

Geophysical Effects of High-Altitude Nuclear Explosions

PROMINENCE has been given recently to some geophysical effects of the nuclear tests carried out in August 1958 at Johnston Island in the Pacific. According to newspaper reports[1], these tests included high-altitude explosions at heights of the order of 100 miles on August 1 and August 12; for each date the approximate time of the explosion was 1050 U.T. Observations[2] at Apia, Samoa, show that the test on August 1 coincided with the appearance of an aurora and the occurrence of radio fade-outs at Apia. The special significance of these phenomena is that Apia and Johnston Island lie approximately at opposite ends of a geomagnetic line of force, and the observations at Samoa have been explained[3] as due to the generation of charged particles by the test at Johnston Island and the subsequent guidance of the particles along the line of force to produce increased ionization in the lower ionosphere at Apia,

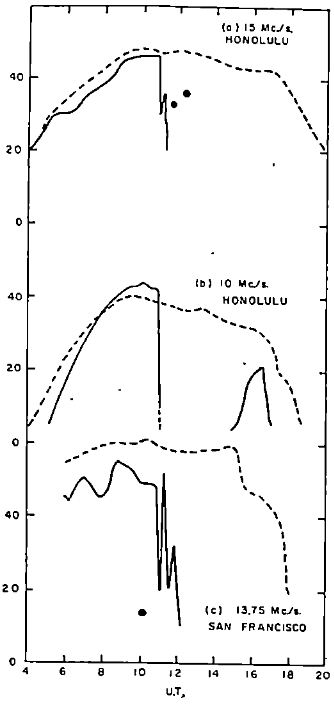

Fig. 1

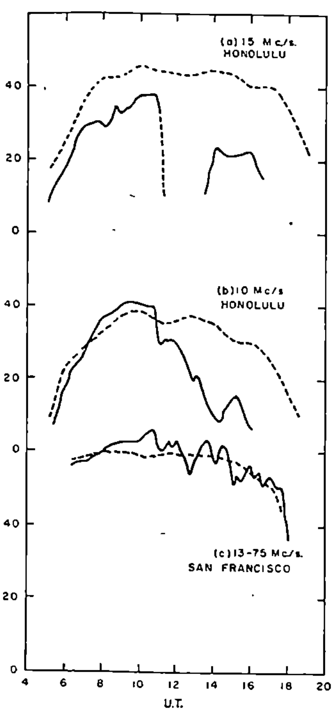

Fig. 2

Fig. 1. Variation with time of signals received at Hiraiso, Japan, on August 1, 1958

Fig. 2. Variation with time of signals received at Hiraiso, Japan, on August 12, 1958

the conjugate point. This mechanism would suggest that any effects are largely restricted to the vicinities of the two ends of the line of force; we wish to present evidence, however, strongly suggesting that increased *D*-layer ionization occurs for distances far greater from the explosion than has hitherto been realized, and at places remote from either the explosion or its geomagnetic conjugate.

Fig. 1 shows the diurnal variation in the strengths of three transmitters as received at the Hiraiso Radio Wave Observatory in Japan; the continuous curve is the record for August 1 and the dotted curve the expected diurnal variation. It may be noted that the time of the explosion coincides with a loss of signal on all three transmitters. The path from Honolulu to Hiraiso passes fairly close to Johnston Island, so that the effects in Figs. 1*a* and *b* are not unexpected. However, the path from San Francisco to Japan is some 3,600 km. from Johnston Island at its nearest point, and, of course, even more remote from the geomagnetic conjugate of Johnston. The records for August 12 are shown in Fig. 2. Again there is a pronounced effect for the Honolulu transmitter on 15 Mc./s. coinciding with the reported time of the explosion, but that on the 10 Mc./s. transmitter is less marked than on August 1, while no significant decrease is detectable for the San Francisco station.

An interesting record is shown on Fig. 3. This is of the integrated level of atmospherics on 28 kc./s. as received at Hiraiso on August 12; an enhancement at the time of the explosion is detectable. The coincidence in time almost certainly implies that the enhancement is due to the nuclear explosion, but there are unusual features. For example, Fig. 3 is dissimilar to the mean diurnal variation of noise on 27 kc./s. shown in Fig. 4, which is derived from Japanese data[4] for August 1957. Normally, one would anticipate the main sources of the atmospherics received in Japan at about 1100 U.T. in August to be in south-eastern Asia and India, with perhaps a subsidiary source, due to the secondary maximum of thunderstorm activity at local dawn, in South America. The enhancement on Fig. 3 could be interpreted as meaning that the source in South America is dominant; that the path of the atmospherics consequently lies close to Johnston; and that the signals are therefore greatly affected. Alternatively, the influence of the explosion may be so widespread as to affect the atmospherics from the thunderstorms in the East Indies, some 7,000 km. from Johnston. A solar flare with its associated sudden ionospheric disturbance could also produce the effect in Fig. 3; there are no reports, however, of such solar activity. Another possibility is a local thunderstorm, but again there are no records of any such storm; incidentally, the 28 kc./s. record for August 1 was completely dominated by thundery activity within Japan. Finally, recent talks at Geneva have shown that the explosion itself can be responsible for the generation of appreciable electromagnetic energy at low frequencies. Many of these alternatives could, of course, be eliminated if conventional wave-form and frequency spectra records for atmospherics were available, particularly if these were coupled with direction-finding and locating systems.

The effects discussed, namely, fade-outs on frequencies of about 10–20 Mc./s. and an enhancement of atmospherics on 28 kc./s., are entirely similar to those accompanying sudden ionospheric disturbance due to a solar flare. The disturbances are known to be caused by the production by the flare of increased

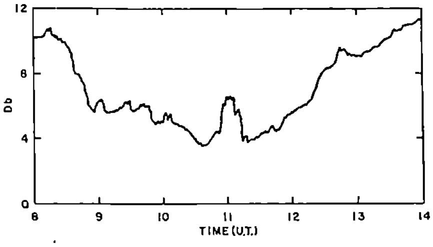

Fig. 3. Variation of atmospheric noise on 28 kc./s. for Hiraiso, Japan, on August 12, 1958

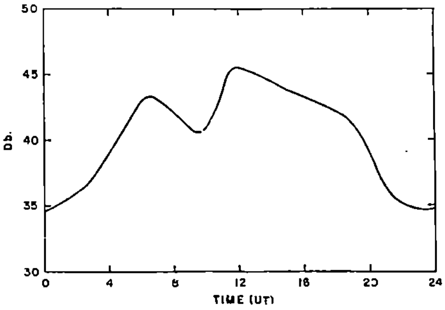

Fig. 4. Mean diurnal variation of atmospheric noise on 27 kc./s. for Japan in August

ionization in the ionospheric *D*-layer. It would appear probable that extra ionization is also produced in the same region by a high-altitude nuclear explosion, perhaps particularly when the explosion lies within the *D*-layer itself (height 70–100 km.). The record of Fig. 1*c* shows conclusively that the effects are not confined to regions influenced by particles guided by the Earth's magnetic field, the mechanism postulated in connexion with the ionization at the geomagnetic conjugate; the addition, incidentally, of precession along a geomagnetic line of latitude[3,5] still implies a considerable restriction in the areas affected. Other mechanisms must therefore also be invoked. Possibilities include analogies with the reported effects of thunderstorms on the ionosphere, including, for example, the direct production of ionization by the electromagnetic radiation of long wave-length generated by the explosion. Again, the production of shock waves with consequent magneto-hydrodynamic influences is feasible; in this connexion the violent oscillations of the record of Fig. 1*c* are intriguing.

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Auroral Isochasms

THEORETICAL reasons exist for believing that the auroral isochasms should be projections of circles in the equatorial plane outside the Earth on to its surface along the geomagnetic lines of force[1].

Such projections have been calculated by Hultqvist[2], taking into account up to the fifth term of the spherical harmonic development for epoch 1945. Four such projections on the northern hemisphere are drawn as solid curves in Fig. 1. The projections are ovals with the longest diameter approximately in the plane containing the 170° and 350° geomagnetic meridians. The ovals converge with decreasing diameters towards the point of intersection of Bartels's eccentric dipole with the Earth's surface[2], to which point the geomagnetic north pole is displaced by the higher terms of the harmonic development.

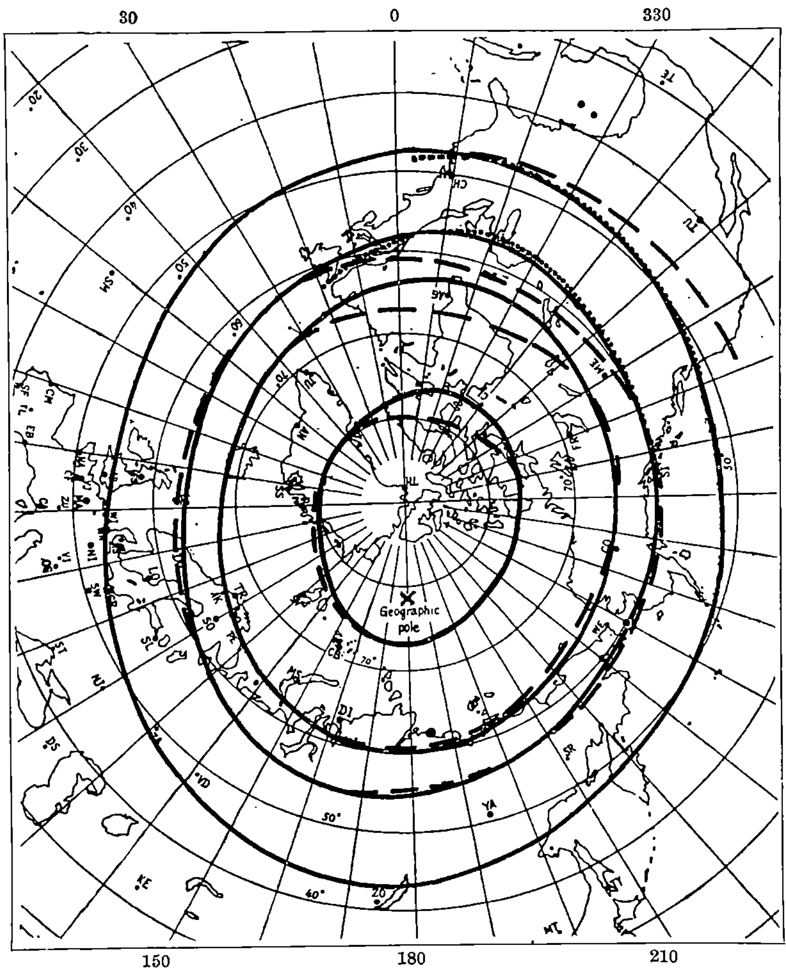

Fig. 1

Some of Vestine's[3] observational isochasms, which closely coincide with the calculated projections over most of the 360° of longitude, are also shown in Fig. 1 (broken lines). It can be seen that for the broken curves the agreement with the theoretical (solid) curves is good except in the region of north-eastern America, where the Vestine curves run up to some 4° too far to the north. The disagreement is so large and so systematic that, on the basis of the curves mentioned, the hypothesis of the isochasms being projections of circles in the equatorial plane seems somewhat doubtful.

Gartlein[4] has recently prepared new isochasms for the territory of the United States based on visual observations made during the International Geophysical Year. Two of those isochasms can be seen in Fig. 1 (dotted lines). They concern just those regions where Vestine's and the calculated isochasms disagree. It is interesting to see that Gartlein's isochasms differ considerably from Vestine's and agree very well with the theoretical curves. Only in the extreme eastern part—chiefly over the sea—do they appear a little too much to the north. The agreement is surprisingly good, especially for Gartlein's southernmost curve, if the uncertainty inherent in the method of evaluation of the observational curves is taken into account.

Thus the agreement between observed isochasms and projections of circles in the equatorial plane along the lines of force seems to be good, in view of the uncertainty mentioned above of the experimental isochasms definitely demonstrated by the disagreement between Vestine's and Gartlein's curves.

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Possible Causes of Geomagnetic Fluctuations having a 6-Sec. Period

WE have delayed comment on F. B. Daniels's letter in *Nature*[1] hoping that we would obtain further information relevant to his suggestion that the fluctuations of about 6 sec. period in the geomagnetic field may be due either to microseisms or microbaroms. Although the general object of our main investigation has been to get a clear idea of the cause and origin of the geomagnetic fluctuations in a wide frequency-range, the main emphasis has been in the normal 'daytime' *pulsations continues* of 10–40 sec. period. The particular record referred to by Dr. Daniels[2] was taken during a magnetic storm, when geomagnetic fluctuations cover a range of periods from fractions of a second up to many minutes.

We have, however, observed that fluctuations in the range of 1–7 sec. period do sometimes appear on our records of $\delta X/\delta t$, $\delta Y/\delta t$ and $\delta Z/\delta t$ nearly simultaneously at two sites some hundreds of miles apart.

We have not attempted to measure microbaroms and would certainly encourage an investigation such as Dr. Daniels suggests, since it is possible that microbaroms are associated with some types of geomagnetic fluctuations. For example, pressure changes in the ionosphere may result from the influx of particulate charged material.

Recently, we have been paying more attention to fluctuations during the hours of darkness and especially during the magnetically quiet time of night. At this time, geomagnetic fluctuations may be associated with particulate matter from the Sun but probably not with direct radiation. We have noted a number of occasions when a characteristic damped fluctuation of about 1–3 min. period and maximum amplitude of ½–2 gamma is readily related to a similar phenomenon simultaneously recorded some hundreds of miles away. However, the most interesting feature is that fluctuations of this type are sometimes associated with oscillations of periods of 2–7 sec. Rarely, these precede the main phenomenon by a minute or so, but more often they accompany it, and may continue for some time if the general magnetic activity is maintained. We believe the short and long periods are associated and both of electromagnetic origin.

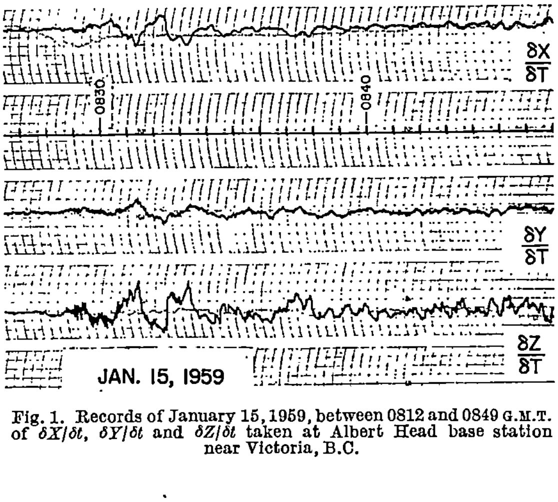

Fig. 1. Records of January 15, 1959, between 0812 and 0849 G.M.T. of $\delta X/\delta t$, $\delta Y/\delta t$ and $\delta Z/\delta t$ taken at Albert Head base station near Victoria, B.C.

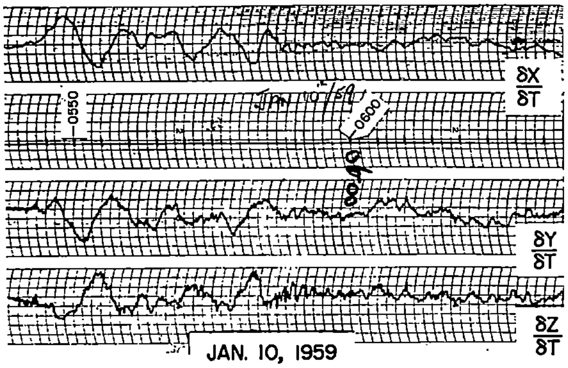

Fig. 2. Records of January 10, 1959, between 0544 and 0610 G.M.T. of $\delta X/\delta t$, $\delta Y/\delta t$ and $\delta Z/\delta t$ taken at Albert Head base station near Victoria, B.C.

Two dates which show the short-period oscillations starting just before the main train are 0819·7 on January 15, 1959, and about 0548·0 on January 10, 1959, G.M.T. We have been informed by Prof. Hugo Benioff that his seismograph records at the California Institute of Technology do not exhibit oscillations starting or increasing at the times and on the days mentioned, and we have not observed any association with the local Dominion Astrophysical Observatory seismograms.

Figs. 1 and 2 show the records at our base station near Victoria, B.C., for the two dates referred to above. The records for $\delta X/\delta t$, $\delta Y/\delta t$ and $\delta Z/\delta t$ are shown. Full scale on each record is about 1 gamma for the longer-period fluctuation. Fig. 3 shows the simultaneous records of $\delta X/\delta t$ at our base station and of $\delta Z/\delta t$ near Borrego Springs about 1,100 miles away in southern California.

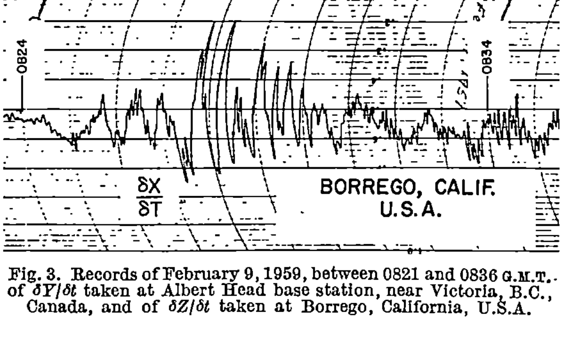

Fig. 3. Records of February 9, 1959, between 0821 and 0836 G.M.T. of $\delta Y/\delta t$ taken at Albert Head base station, near Victoria, B.C., Canada, and of $\delta Z/\delta t$ taken at Borrego, California, U.S.A.

It is probable that these fluctuations are associated with the 'oscillatory bursts' in earth-current records examined by V. A. Troyiçkaya. These, she states, are persistently associated with characteristic (magnetic) oscillations having a period of the order of 2–3 sec.[3].

The longer-period damped fluctuations are of interest in another respect. Examination of the magnetograms of the local Dominion Observatory, of which Mr. Bernard Caner has kindly supplied copies, shows that these damped fluctuations can often be recognized on the magnetograph records as a very sudden and small displacement of *H*, *D* and *V* (from 1 gamma upwards). While these displacements may be seen by looking for them at the times suggested by the fluctuation records, the reverse procedure is not very effective.

It is difficult and costly for us to record the geomagnetic fluctuations at far distant places when we are dependent on transport of heavy equipment. Thus we have not operated simultaneously a pair of stations much more than 1,000 miles apart. We believe, however, that this type of fluctuation, which is most obvious in the early part of the night when the general activity is low, may be shown on the magnetograms of observatories covering a large area. We think this examination should be made and will willingly supply dates and times when these fluctuations have been recorded at our base station within the past few months.

This work is supported by the Defence Research Board of Canada and is part of the programme of the Pacific Naval Laboratory.

H. J. Duffus
J. A. Shand
Charles Wright

Pacific Naval Laboratory,
Esquimalt, B.C.

---

[1] Daniels, Fred B., *Nature*, **182**, 1439 (1958).

[2] Duffus, H. J., Nasmyth, P. W., Shand, J. A., and Wright, Sir Charles, *Nature*, **181**, 1258 (1958).

[3] Troyiçkaya, V. A., *Dok. Akad. Nauk, U.S.S.R.*, **91**, 2, 241 (1953). Translation *T174R*, 6, by Hope, E. R., Defence Research Board, Ottawa.

Origin of Sodium and Lithium in the Upper Atmosphere

Lithium resonance radiation in the twilight airglow of the southern hemisphere has recently been observed in several places[1,2]. Over Adelie Land in the Antarctic this radiation is reported to have been present both in 1957 and 1958. In October 1957 its intensity was estimated visually to be of the order of a tenth that of the sodium *D* lines in the twilight. After the high-altitude nuclear bomb explosion in the Pacific in August 1958 this radiation was also observed at Hallett Station in the Antarctic and afterwards in September at Invercargill in New Zealand. Its intensity is roughly estimated as equal to the total sodium *D* line intensity at Hallett in August and a tenth of this in New Zealand in September.

An attempt has been made to estimate the ratio of free lithium to free sodium from the intensity ratios found[3]. This estimate was based on the assumption that, apart from a factor of 17 arising from the presence of the Fraunhofer *D* lines in the solar spectrum and slightly different oscillator strengths, the abundance ratio is equal to the intensity ratio. The conclusion reached is that the ratio of the abundance of lithium to sodium is of the order of 0·006 (perhaps even 0·02 if ions are also considered). Compared with a ratio of 0·002 expected if the common origin of these elements in the Earth's atmosphere is meteoric debris, and a ratio of $2{\cdot}3 \times 10^{-5}$ expected if their origin is in sea water, the result is taken as strong evidence for the meteoric source.

Similarly, from the New Zealand and Hallett observations an attempt has been made to estimate the amount of lithium in the atmosphere, again on the assumption that sodium and lithium intensities in the twilight airglow are proportional to their abundances[2]. This calculation takes an old estimate of 6×10^9 atoms/cm.^{2} for the abundance of sodium and suggests that the quantity of lithium in the upper atmosphere fell from 20 kgm. to 2 kgm. between August 5 and September 5.

Because of resonance absorption of sunlight in the layers, the assumption of linearity is a very poor one, however, at least in the case of sodium[4]. In fact, the increase of intensity of scattering with abundance becomes significantly less than linear for abundance of sodium in excess of 10^9 atoms/cm.^{2}. In the neighbourhood of 25×10^9 atoms/cm.^{2}, the intensity actually passes through a maximum and declines very slowly for larger quantities of sodium. This non-linearity makes any estimate of the lithium–sodium abundance ratio impossible from the intensity ratios alone. An absolute determination of the quantity of one or the other present is also necessary. Even then the double value in the intensity abundance curve may leave the situation ambiguous.

The season for which the lithium observations are reported was late winter. This is the very time when the seasonal maximum in sodium abundance would be expected. In the northern hemisphere there occurs a sodium maximum at the inland station of Saskatoon in Canada of about 10×10^9 atoms/cm.^{2} in late February. At Haute-Provence Observatory in southern France intensity peaks corresponding to abundances in the neighbourhood of 25×10^9 atoms/cm.^{2} are reached in December and March. Between these intensity maxima lies a minimum in February with which abundances as low as 5×10^9 atoms/cm.^{2} and higher than 100×10^9 atoms/cm.^{2} are consistent because of the maximum in the abundance-intensity curve.

If the sodium in the southern hemisphere behaves similarly, and particularly if the seasonal variation is like that observed in France, sodium abundances from 5×10^9 atoms/cm.^{2} to more than 100×10^9 atoms/cm.^{2} cannot be excluded in August. For this range of abundance the variation of intensity is so small that any quantity of sodium between these limits would be consistent with $3/17 \times 10^8$ atoms of lithium/cm.^{2} and an intensity ratio of the order of 0·1. From the measurements available, therefore, it is safe to conclude only that the lithium–sodium ratio lay somewhere between 0·006 and 2×10^{-5} or, more probably, between 0·0035 and 0·0006.

Of course, the Johnson Island nuclear explosion on August 1, 1958, may very well be the source of at least part of the lithium observed[5]. Lithium–sodium intensity measurements as a consequence have become even less useful in solving the problem of the origin of the atmospheric sodium.

On this question there are three pieces of evidence, none of them conclusive. There were the repeated observations from southern France during 1955 and 1956 of much more sodium towards the Atlantic Ocean than towards the Continent[4]. There is a remarkably different seasonal variation in sodium near the ocean than is found far inland, with much more sodium near the ocean[6]. Finally, there is the recent attempt by Lytle and Hunten[7] to detect the resonance lines of potassium in twilight. This places an upper limit of 1 : 40 on the potassium–sodium ratio, whereas sea water has a ratio of 1 : 47 and all other sources between 1 : 10 and 1 : 5. At this time the evidence must be taken as favouring a marine origin.

The work reported here was supported in part by a grant from the National Science Foundation.

T. M. Donahue

Department of Physics,
University of Pittsburgh,
Pittsburgh 13, Pennsylvania.
April 20.

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[1] Delannoy, J., and Weill, G., *C.R. Acad. Sci., Paris*, **247**, 806 (1958).

[2] Gadsden, M., and Salmon, K., *Nature*, **182**, 1598 (1958).

[3] Barbier, D., Delannoy, J., and Weill, G., *C.R. Acad. Sci., Paris*, **247**, 886 (1958).

[4] The consequences of this fact have been treated in a series of papers by Blamont and Donahue, Chamberlain and Hunten and by Galperin and their collaborators. References may be found in Blamont, J. E., Donahue, T. M., and Stull, V. R., *Ann. Geophys.*, **14**, 253 (1958); Chamberlain, J. W., Hunten, D. M., and Mack, J. E., *J. Atm. and Terr. Phys.*, **12**, 153 (1958) and Galperin, G. I., "The Airglow and the Aurorae", 95, edit. by Armstrong and Dalgarno (Pergamon Press, London, 1956).

[5] Barber, D. R., *Nature*, **183**, 384 (1959).

[6] Blamont, J. E., and Donahue, T., *C.R. Acad. Sci., Paris*, **247**, 496 (1958).

[7] Lytle, E. A., and Hunten, D. M., *J. Atm. and Terr. Phys.* (in the press); I wish to thank Dr. Hunten for an opportunity to see his results before publication.

Effect of Cathode Inclusions on Electrical Discharges

Recognition has been given for some considerable time now to the fact that the surface of the negative electrode in a spark gap can influence the electrical discharge[1]. An attempt has been made to ascertain the location of the starting place of arc spots in relation to the metallurgical features of the cathodes.

As is well known, metals frequently contain microscopically visible inclusions often of more than one type chemically. In stainless steels, with which we have been principally concerned, oxides, nitrides, carbides, slag particles and pieces of refractories are the major inclusions.

Microscopical examination of clean polished specimens which had been used as negative electrodes in a small experimental spark gap showed that metal had vapourized from around certain inclusions, the bulk of the material being unaffected. It is of considerable interest to note that the inclusions affected possessed low electrical conductivity whereas inclusions of relatively good conductivity were entirely unaffected.

This phenomenon is by no means peculiar to stainless steels. For example, localized damage has been found around cuprous oxide inclusions in samples of copper. Cuprous oxide also has a low electrical conductivity. The current passing in these experiments under non-arcing conditions was approximately $1\cdot6 \times 10^{-4}$ amp. cm.$^{-2}$ and the minimum resistivity for arc initiation appears to be 10^3 ohm. cm.

This work, which forms part of a programme to investigate surface properties of metals, is to be reported in detail elsewhere.

P. C. L. Pfeil
L. B. Griffiths

Metallurgy Division,
Atomic Energy Research Establishment,
Harwell, Berks.
April 3.

---

[1] See, for example, Jones, F. Ll., "The Physics of Electrical Contacts" (Oxford Univ. Press, 1957).

X-ray Spectrographic Determination of Strontium

Roberts[1] recently described an X-ray fluorescence spectrographic method for the determination of strontium in animal bone using the Philips *PW* 1520 spectrograph fitted with a quartz analysing crystal. In our laboratories a lithium fluoride crystal was available and was used for similar analyses since, compared with a quartz crystal, it increases the intensity of the strontium *Kα* line by a factor of 2·8 and the line/background ratio by a factor of 1·15. Thus the counting time to achieve a given coefficient of variation (due to the counting statistics) can be reduced by a factor of 3·5 or, if the same counting time is compared, the coefficient of variation can be reduced by a factor of 1·9, by using the lithium fluoride crystal.

The instrumental conditions were: Philips X-ray spectrograph, *PW* 1520; tungsten target tube, 48 kV., 20 m.amp.; argon-filled Geiger counter; X-ray path evacuated; exit collimator not fitted. Samples were prepared in a manner similar to that described by Roberts, but the 'Mylar' film was not removed from the sample holder because of the potential danger of contamination of the window of the X-ray tube. The absorption of the strontium radiation by this film is theoretically about 0·1 per cent and, in practice, was not detected.

The specific intensity of the strontium *Kα* line from milk powder ash was found to be identical with that from animal bone ash, and results obtained by several different methods for both these types of sample are compared in Table 1.

Table 1

Sample	Strontium content (p.p.m.)			
	X-ray spectrography	Emission spectrography (ref. 2)	Neutron activation*	Flame photometry (ref. 2)
Bone ash				
1	90	90	89	89
2	120	109	—	124
3	198	190	—	192
4	340	345	—	335
Milk ash				
1	33	36	33	32
2	34	31	32	33
3	56	45	53	51
4	65	64	65	64

* Determinations carried out by Dr. G. E. Harrison and Mrs. E. Sowden, Medical Research Council Radiobiological Unit, Atomic Energy Research Establishment, Harwell.

Since these determinations were carried out, a molybdenum-target X-ray tube has been obtained and shown to increase the intensity of the strontium line by a factor of 1·5 and improve the line/background ratio by a factor of 2·5. Thus with this tube and a lithium fluoride crystal it is possible to determine 10 p.p.m. strontium in bone or milk powder ashes in 30 min. with a coefficient of variation due to the counting statistics of 10 per cent.

J. T. Campbell
H. I. Shalgosky

U.K. Atomic Energy Authority (Research Group),
Chemistry Division,
Woolwich Outstation,
C.37 Royal Arsenal,
Woolwich,
London, S.E.18. April 4.

---

[1] Roberts, W. M. B., *Nature*, **183**, 887 (1959).

[2] Jury, R. V., Webb, M. S. W., and Webb, R. J., U.K. Atomic Energy Authority Report No. *C/R* 2614 (Nov. 1958).

FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Tuesday, May 26

University of London (at Imperial College of Science and Technology, South Kensington, London, S.W.7), at 5.30 p.m.—Prof. W. O. James, F.R.S.: "Botany—Here and Now".* (Inaugural Lecture.)

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Mr. A. F. Shore: "Animals in Ancient Egypt".* (Fourth of six lectures on "Animals in Archæology". Further lectures on June 2 and 9.)

Tuesday, May 26—Friday, June 5

National Union of Teachers (at the National Hall, Olympia, London)—National Education and Careers Exhibition.*

Wednesday, May 27

Royal Statistical Society (at the London School of Hygiene and Tropical Medicine, Keppel Street, Gower Street, London, W.C.1), at 5 p.m.—Dr. J. Kiefer: "Optimum Experimental Designs".

Society of Chemical Industry, Food Group (at 14 Belgrave Square, London, S.W.1), at 6.15 p.m.—Annual General Meeting, followed by Dr. J. R. Nicholls: "Food and Ordinary Man".

Jephcott Lectures Trust (at the Royal Society of Medicine, 1 Wimpole Street, London, W.1), at 7 p.m.—Sir Alexander R. Todd, F.R.S.: "Nucleic Acids and their Role in Future Chemotherapy of Tumours and Virus Diseases" (First Jephcott Lecture).

British Psychological Society, Medical Section (in the House of the Royal Society of Medicine, 1 Wimpole Street, London, W.1), at 8.30 p.m.—Dr. Henri Rey: "Studies on the Relationship of Hormones, Brain Activity and Behaviour in Women".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. Sir Harold Spencer Jones, F.R.S.: "Some Principles of Clock and Watch Design".

Thursday, May 28

University of London (at the Postgraduate Medical School of London, Ducane Road, London, W.12), at 4 p.m.—Dr. E. E. Pochin: "The Therapeutic Use of Radio-iodine".*

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. R. P. Bell, F.R.S., and Mr. T. Spencer: "Kinetics of the Base-Catalysed Bromination of Ethyl Nitroacetate"; Mr. C. F. Cullis, Mr. F. R. F. Hardy and Mr. D. W. Turner: "The Point of Oxygen Attack in the Combustion of Hydrocarbons. II: The Formation and Origin of Ketones".

Institute of Metals (at 17 Belgrave Square, London, S.W.1), at 6.30 p.m.—Prof. N. J. Petch: "The Atomic Mechanisms of Fracture".

Friday, May 29

University College, Department of Mathematics (in the Eugenics Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. R. Thom (University of Strasbourg): "General Position and Transversality".*

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Lecturer in Civil Engineering—The Registrar, The University, Sheffield (May 30).

Lecturer (with a university degree, and preferably previous forensic experience) in Forensic Chemistry in the Department of Forensic Medicine—The Secretary, The University, Edinburgh (May 30).

Map Curator and Cartographer (graduate in geography with a special interest in cartography and map preparation) in the Department of Geography—The Registrar, University College, Singleton Park, Swansea (May 30).

Demonstrator (with a good honours degree in physiology, biochemistry or chemistry) in Chemical Physiology—The Registrar, The University, Manchester 13 (June 1).

Assistant Librarian (with a university degree)—The Secretary, The University, Aberdeen (June 5).

Lecturer (specialized in parasitology) in the Department of Zoology—The Registrar, The University, Hull (June 6).

Assistant Lecturer (preferably with a knowledge of embryology or vertebrates) in the Department of Zoology—The Registrar, University College of Wales, Aberystwyth (June 12).

Lecturer or Assistant Lecturer in Electronics—The Secretary and Registrar, The University, Southampton (June 12).

Electron Microscopist (graduate in medicine, biology or physics, and experienced in the operation and maintenance of a high-resolution instrument (preferably Siemens) and in the techniques of specimen preparation) in the Department of Physiology and Histology—The Registrar, The University, Liverpool (June 13).

Lecturer and an Assistant Lecturer in Physics—The Registrar, The University, Hull (June 13).

Demonstrator (with a degree in agriculture or an honours degree in pure science followed by an adequate postgraduate qualification in agriculture, and preferably some training in field experimentation)—The Secretary, School of Agriculture, The University, Downing Street, Cambridge (June 15).

Scientific Officer (with a good honours degree in botany and preferably experience in plant physiological research) in the Botany Department, for work on the physiology of the sugar beet plant, especially on the causes of variation in yield of field crops—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (June 15).

Electronic Computing Engineer (university graduate experienced in the development and design of electronic computing equipment) on the staff of the Adolph Basser Computing Laboratory in the School of Physics, to assume responsibility for a part of the development programme—The Registrar, University of Sydney, Sydney, N.S.W., Australia (June 19).

Assistant Experimental Officer (with a degree in a biological subject and practical experience in bacteriological methods and techniques), for work on the ecology of soil micro-organisms—The Secretary, Rothamsted Experimental Station, Harpenden, Herts (June 30).

Botanist (with an honours degree in botany from a recognized university and preferably at least two years postgraduate experience), for duties particularly concerned with the study of the growth characteristics of the tea bush in the chief soil-climatic regions of East Africa, the study and provision of improved planting material, and the botanical interpretation of field experiments—The Director, Tea Research Institute of East Africa, P.O. Box 91, Kericho, Kenya Colony (June 30).

Research Assistants (with an honours degree of a British university or equivalent qualification) in Plant Biochemistry, Electrical Engineering, Applied Physics, Mechanical Engineering, Applied Chemistry, Mining, and Biochemical Microbiology—The Principal, Heriot-Watt College, Edinburgh (June 30).

Soil Scientist (with a Ph.D. degree in soil chemistry and preferably with some experience), to carry out soil fertility investigations, both applied and fundamental, in relation to tobacco, and to supervise soil analysis—The Director, Tobacco Research Board of Rhodesia and Nyasaland, P.O. Box 1909, Salisbury, Southern Rhodesia (June 30).

Assistant Lecturer (Grade B) in Chemistry—The Principal, Peel Park Technical College, Salford 5.

Chair of Engineering—The Registrar, The University, Leicester.

Head (with high academic qualifications, and experience of full-time teaching, together with industrial and/or research experience) of Physics and Mathematics Department (Grade IV)—The Registrar, Portsmouth College of Technology, Portsmouth.

Lecturer in Forestry—The Principal, Royal Agricultural College, Cirencester.

Physicist, Basic grade (with a first- or second-class honours degree), for routine and development work in hospital physics—The Secretary, Lambeth Hospital, Brook Drive, London, S.E.11.

Plant Pathologist (with a good honours degree in botany or plant pathology and approved postgraduate training) in Kenya, for laboratory and field research work on the identification and control of plant diseases—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/7/030.

Plant Pathologist (with a good honours degree in botany and with two years postgraduate experience in plant pathology) in the Department of Agricultural Research, Federation of Nigeria, for research into virus diseases of food crops—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/14/035.

Special Officer (Statistician) (with a good honours degree, preferably in agriculture, with at least two years suitable postgraduate training or experience in statistics) in the Northern Region of Nigeria, to advise on the design and supervise analysis and presentation of results of experimental work for all sections of the Research Branch of the Northern Region Department of Agriculture, and to take part in the development of satisfactory experimental techniques in the field—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/408/032.

REPORTS and other PUBLICATIONS

(*not included in the monthly Books Supplement*)

Great Britain and Ireland

Association of Universities of the British Commonwealth. Report of the Executive Council together with the Accounts of the Association for the year 1st August, 1957 to 31st July, 1958. Pp. 25. (London: Association of Universities of the British Commonwealth, 1959.) [272

Ciba (A.R.L.), Ltd. Technical Notes No. 194 (February, 1959): Aerolite in Schools and Colleges. Pp. 8. (Duxford: Ciba (A.R.L.), Ltd., 1959.) [272

The Carnegie Trust for the Universities of Scotland. Fifty-seventh Annual Report for the year 1957–58, submitted by the Executive Committee to the Trustees on 23rd February 1959. Pp. iv+74. (Edinburgh: Carnegie Trust for the Universities of Scotland, 1959.) [272

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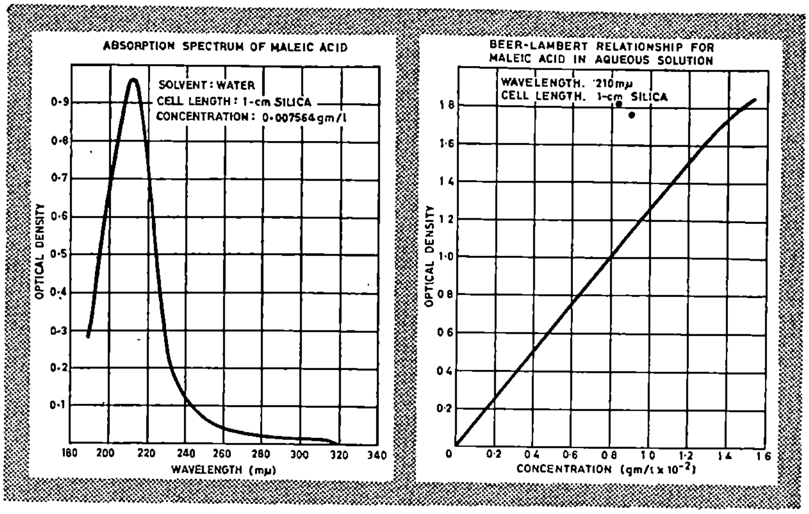
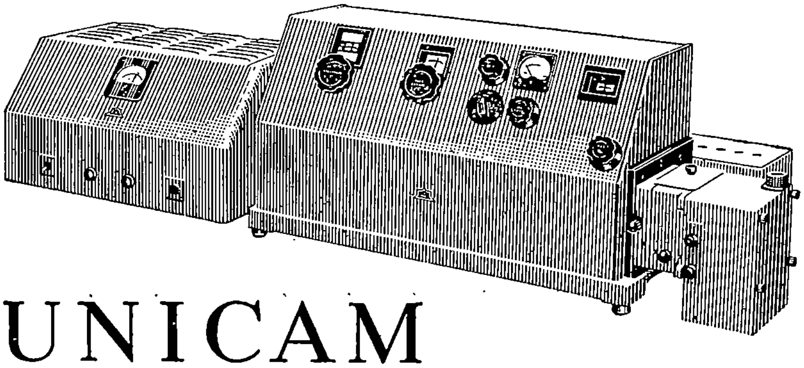


High performance at Low wavelengths

The absorption spectrum of maleic acid reproduced here emphasises the excellent performance of the SP.500 spectrophotometer at low wavelengths. The second graph shows the Beer-Lambert relationship at 210mμ, and illustrates the virtual freedom from stray light at this wavelength.

With the new fused silica prism, the SP.500 Spectrophotometer reaches still further into the ultraviolet—down to 186mμ, the limit set by the absorption bands of atmospheric oxygen. The advantages of this are two-fold: a new region, hitherto accessible only to specially prepared instruments is made available for every user, and the performance of the instrument, over the whole of the important 200mμ—240mμ region, reaches a new high level. The standard test specification for the SP.500 now stipulates not more than 0.2% stray light at 200mμ—a clear indication of the instrument's quality.



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CALCUTTA.

RECRUITMENT IN GOVERNMENT SERVICES AND SECURITY REGULATIONS

THE White Paper dealing with defence is this year entitled "Progress of the Five-Year Defence Plan"* and is much shorter than last year's White Paper. "Defence Statistics 1959/60"†, however, have been collected in a separate White Paper, and there was also issued, in July 1958, a further White Paper, "Central Organisation for Defence"‡. The Defence Budget is given as £1,502·13 million net, of which £585·46 million is on research and development. There is no separate entry under this heading for the Ministry of Defence, but for the Admiralty, the War Office, the Air Ministry and the Ministry of Supply the respective net figures for research and development are £169·03 million, £53·68 million, £213·85 million and £148·90 million. Gross expenditure under this heading by the Ministry of Supply is £521·60 million.

Despite these figures there is, however, no other specific reference to research in any of these White Papers. There is, in the one reporting on progress, a reference to the valuable exchange of information with the United States which has permitted important technical advances to be made in the design of nuclear war-heads, and it is stated that after a recent review of the British ballistic rocket programme, in the light of technical developments in Britain and in the United States, the Government reached the conclusion that, on present knowledge, *Blue Streak* is the type of missile best suited to British needs. It is obvious that the modernization of the Fleet and the re-equipment of the Army are both based on much technological research, but the magnitude of this effort is nowhere disclosed, nor is there any indication as to how effectively it is co-ordinated.

On the Defence Research Policy Committee there is again silence, nor is the Committee even mentioned in the White Paper dealing with the central organization for defence. The latter paper formally announces the confirmation, as a result of eighteen months experience, of the re-organization of the Ministry of Defence announced by the Prime Minister on January 24, 1957, with the introduction of three new features. First, the composition and operation of the Defence Committee of the Cabinet are being adjusted to secure greater flexibility and efficiency. Secondly, a Defence Board is being set up to assist the Minister of Defence in formulating a defence policy and in dealing with inter-Service problems. Some adjustments are also being made in the staff organization, including the creation of a new post, Chief of the Defence Staff, in place of the existing combined posts of Chairman of the Chiefs of Staff Committee and Chief of Staff to the Minister of Defence. The holder of this post will be responsible to the Minister of Defence and will be his principal military adviser. He will also be a member of the Defence Board, of which the Minister of Defence will be chairman. The other members of the Board are the Ministers for the three Service Departments, the Minister of Supply, the Chief of the Naval Staff, the Chief of the Imperial General Staff, the Chief of the Air Staff, the Permanent Secretary of the Ministry of Defence and the Chief Scientist of the Ministry of Defence. As already noted, there is no reference to the Defence Research Policy Committee, nor, although in the defence statistics the interrelation of defence and civil expenditure is fully recognized, to the Advisory Council on Scientific Policy. Formal or even informal arrangements for the correlation of defence and civil requirements in the research and development effort in Britain appear to be lacking.

This aspect of the defence effort was scarcely discussed in the subsequent Parliamentary debates although the dependence of effective defence on scientific and technical advance was generally recognized. There was, however, a significant admission by the Minister of Supply, Mr. Aubrey Jones, in replying for the Government in the debate in the House of Commons on February 26. While the Minister of Defence had given most encouraging accounts of recruitment to the Armed Forces, Mr. Jones admitted he could not be quite so encouraging about the recruitment of scientists to the Government's defence establishments. He could offer no improvements in pay or amenities, but he hoped that due advantage would be taken of the unrivalled opportunities for research which he could offer.

Even more significant, however, was Vice-Admiral J. H. Hallett's reference to secrecy. . Vice-Admiral Hallett was concerned primarily with the modernization of the Fleet and whether this was being carried out appropriately for the functions it would perform, particularly in respect of the defence of communications and the threat of submarine warfare. He pointed out, however, that no one outside a small circle of Service officers, Government officials and possibly senior Ministers could hope to answer the vital questions because they did not possess the information which is the essential basis of any opinion worth while.

That is equally true of any other section of defence policy, and Admiral Hallett reminded the House of Commons that this is a novel and dangerous position. In the past, military thinking in Britain has been enriched by the contributions of people outside the Services, outside the Government and outside politics and public life altogether. Often such contributions have profoundly influenced the thought of junior officers, who incidentally themselves had access to the information on which to reach independent judgments of their own.

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* Progress of the Five-Year Defence Plan. Pp. iii+7. (Cmnd. 662.) (London: H.M. Stationery Office, 1959.) 9*d*. net.

† Defence Statistics 1959/60. Pp. 8. (Cmnd. 661.) (London: H.M. Stationery Office, 1959.) 9*d*. net.

‡ Central Organisation for Defence. Pp. 6. (Cmnd. 476.) (London: H.M. Stationery Office, 1958.) 6*d*. net.

That, said Admiral Hallett, has all changed, and although such writers are still to be found, their contributions are now based essentially on guesswork, and very few people indeed possess the vital information without which the study of tactics and strategy is waste of time. The great danger, moreover, is that the handful of experts who alone possess the information are not necessarily the people best qualified to interpret it. Admiral Hallett illustrated this by our experience in the development of radar, when the secrecy with which this was developed led to its applications in naval warfare being overlooked, and he urged the Government to consider very seriously whether the present secrecy is any longer in the true interests of national security.

The impossibility of any effective discussion of the scientific and technical aspects of defence policy in the light of information publicly available was pointed out in these columns in commenting on the White Paper on defence last year. It is obvious that Admiral Hallett is uneasy as to the situation from the Services point of view and his disquiet is based, moreover, on his experience as vice-controller of the Navy and as second-in-command of the Anglo-American Striking Fleet. Indeed, experience in the latter post made him particularly anxious as to the effect of secrecy on the Anglo-American exchange of scientific and technical experience.

These comments seem to reinforce doubts as to whether the Defence Research Policy Committee is functioning effectively, and as to its relations with the Advisory Council on Scientific Policy. Even with adequate informal contacts, the present structure appears to place an excessive responsibility on the common chairmanship, and makes informal discussion in scientific and technical circles not merely desirable but even essential. This is as important from the point of view of efficient use of the limited resources of Great Britain both of materials and of man-power as it is from that of the wise direction of policy, and would go far to establish the public confidence which is always an essential element in effective defence. To say the least, Mr. Orr-Ewing's reply to a question to the Minister of Defence on April 8 as to what consideration the Defence Research Policy Committee has given to the effect of the resignation of scientific research workers as a result of the uncertainty of Government policy is not helpful. Conformity with established practice is no longer a sufficient reason for secrecy and a refusal to promote public discussion. Secrecy may be one reason why the Minister of Supply finds it difficult to recruit sufficient scientists for his research establishments. Even unrivalled material facilities and equipment will not attract first-class minds if they are doubtful as to the value of their work, or the possibility of the free discussion of results among their fellows with the cross-fertilization of minds upon which scientific advance depends.

PRESENT TRENDS IN BOTANICAL STUDIES

Vistas in Botany

A Volume in Honour of the Bicentenary of the Royal Botanic Gardens, Kew. Edited by Dr. W. B. Turrill. (International Series of Monographs on Pure and Applied Biology. Division: Botany, Vol. 2.) Pp. xv+547. (London and New York: Pergamon Press, 1959.)

An occasion such as the bicentenary of the Royal Botanic Gardens, Kew, offers a rare opportunity to take stock of the present position in botany and of desirable trends for the future [see also p. 1488 of this issue]. The present volume, edited by W. B. Turrill, represents an attempt to do this. It consists of surveys of different facets of botanical inquiry by well-known authorities, and though perhaps it emphasizes those aspects of the subject which have especially been the pre-occupation of Kew, it covers so wide a field that there are few botanists who will not feel constrained to consult its pages and few who will put it down without having profited by its perusal.

Without any wish to make invidious comparisons, which would indeed require unprecedented knowledge in a variety of subjects, it is evident that the distinguished authors of these pages have looked at their limited fields in very diverse ways. Some have succeeded in discovering and presenting a fair and attractive vista; others perhaps have scarcely been able to see the wood as a whole but have not missed a tree, while still others have been so interested in the first tree that they have scarcely gone beyond it. In each of the several styles there is at least one example which is masterly of its kind, and the diversity of treatment adds piquancy to one's reading and is a welcome change from the monotony of a series of 'reviews of the present position'.

The plan of the work thus is a series of surveys of the main groups of plants coupled with special statements about the more general botanical problems. There is a historical preface by the Editor, and the first paper is a short introductory one by the present director of the Royal Botanic Gardens, Kew, Dr. George Taylor.

The massive contributions of Kew to taxonomy justify pride of place being given to an article on this subject by H. J. Lam. This ranges widely over what may perhaps be called the basic theories underlying classification, taxonomy and systematics, with a sufficiently individual point of view, perhaps fundamentally classical and morphological, to integrate wide reading with interesting and suggestive reflexion. Rudolfo E. P. Pichi-Sermolli also accepts taxonomy as the synthesis of all biological knowledge and exemplifies this point of view in his exhaustive treatment of the Pteridophyta, in which, after surveying the development of present knowledge, he delves deeply into the problems of phylogeny in the various taxa of this great group. In dealing with the Gymnosperms, W. B. Turrill, apart from a discussion of the 'telome' hypothesis, has to accept the limitations due to modern conceptions of the Gymnosperms as a group of phyla offering vistas of several diverse types, in which the peculiarities of the reproductive systems in comparison with the Angiosperms occupy a prominent place. P. W. Richards records much of interest in the Bryophyta, especially to ecologists and morphogeneticists, in relation to the developmental stages, the alternation of forms and their evolution. The Algae are considered by W. R. Taylor, "Phycology in Retrospect and Anticipation", who directs attention to the enormous gaps existing even in the taxonomy of the group from which the higher plants must have evolved. Particularly can one note the lack of an organized embryology and even of essential cytological detail. In contrast there is a high degree of knowledge in some limited fields of algal physiology, ecology and utilization. C. T. Ingold's admirable survey of the very extensive literature on Fungi shows how much studies of this group have contributed to general botanical problems, particularly perhaps those of sex and inheritance, while the physiology of their nutrition has much to give to problems of morphogenesis through hormone control, as well as to knowledge of antibiotics. K. A. Bissett has faced with success the difficult task of treating the bacteria as organisms rather than as biochemical or medical entities.

While the study of the larger groups of plants and their taxonomy has been pursued for many years, that of the viruses, if indeed they are to be classified as plants, is comparatively recent, and as F. C. Bawden points out, has only made much progress in the past two or three decades with the rapid advances in the chemical and physical methods developed for enzymology. The fascinating story of their crystal structure and intimate relation to other nucleoproteins has made the viruses of even greater interest to the general biologist than to the plant pathologists who first recognized them. This is equally true of the details of cytological structure revealed by D. G. Catcheside, who, switching skilfully from cytoplasm to chromosomes and bacteriophage, marshals the evidence that deoxyribonucleic acid is the significant part of the nucleus providing genetic information. These two papers are, in fact, a valuable source of ideas for those not very familiar with rapidly advancing fields of work. Also essentially analytical in outlook is the article on biochemistry by E. C. Bate-Smith. Perhaps the most interesting part of this is an appreciation of the possibilities of comparative biochemistry in plants which, it is thought, will be based on secondary products rather than those common to all organisms. The useful biochemical processes for the purpose of phylogenetic comparisons would thus be those present in a series of forms, but lost and not regained in their successors, as apparently may be the case in some of the leucoanthocyanins.

A long period of inertia followed the early anatomical discoveries of Grew and Malpighi, and in tracing the re-development of plant anatomy, C. R. Metcalfe illustrates the leading part played by the Jodrell Laboratory at Kew in Great Britain. Perhaps more important than his plea for "brighter" anatomy teaching is the need he stresses for organizing the enormous amount of material which must be available for comparative use, particularly perhaps in the Angiosperms. Another subject, palæobotany, profited greatly from the activities of the Jodrell Laboratory under D. H. Scott, and indeed from the fact that three of the directors of Kew, Sir Joseph Hooker, Sir Arthur Hill and Sir Edward Salisbury, have engaged in palæobotanical research. John Walton's sympathetic account of the personalities who have led the way in this field in Britain, and of their views, must be in many ways the best of the pure 'vistas', Sewardian in quality.

If some of the more modern aspects of the subject illustrate the value and the use of the analytical method, the considerable paper, "Genes, Chromosomes and Evolution", by G. L. Stebbins, offers in contrast an approach through the widest fields of cytogenetics and floristics which has also become popular in the past twenty years and which aims at integrating the facts of distribution, taxonomy and cytology in terms of the most recent genetical theory. Plant geography, as W. B. Turrill shows in a notable and comprehensive treatment, also integrates a great deal of material of general and evolutionary interest, as well as seeking to classify distributional units and arrange them in provisional and more useful hierarchies. The characteristics of plant sociological units and their groupings are considered in greater detail by J. Braun-Blanquet ("Grundfagen und Aufgaben der Pflanzensociologie") together with their relations to synecology, to community succession and (somewhat sceptically) to statistics. Causal plant ecology is treated by a former director of Kew, Sir Edward Salisbury, who considers it as running parallel to physiology, the relation of plant growth to physical and chemical environmental characters, but subject to the additional stresses imposed by competition. In these circumstances, extremes of environment, particularly in relation to phases of growth, are often more decisive in nature than average conditions, while rooting conditions are especially important in competition. Appropriately in this connexion, the paper on plant physiology by F. A. C. Went lays emphasis on the control of plant growth by temperature regimes, by photoperiodism, and by hormones, as well as directing attention to the tendency to locate individual chemical processes in special localities, either in the cell or in special sites in the tissues.

A comprehensive volume of this type will always leave the reader with at least some impressions about the subject surveyed. Biologists can rarely get far away from the central topics of evolution and taxonomy, nowadays perhaps accompanied by the study of the mechanisms of heredity, and these ensure a considerable integration of any large series of general botanical papers such as this. But the reader is also made aware of what is becoming an increasingly important aspect of biological work, the physical difficulty, to say nothing of the intellectual one, of maintaining an organization in which the vast accessions of material and knowledge can be stored in a readily available form and integrated for general use. It seems without question that this is only possible in an institution such as that at Kew, and one is able to appreciate properly how an organization based on gardens, herbaria and laboratory has done so much for taxonomy in particular and for botany in general. Whether this is the organization most suitable for the widest type of integration is no doubt a question which would require very detailed discussion. Perhaps the second point emerging from this survey of the botanical field is the very large gap remaining in our knowledge of the relations between growth and morphological development, and particularly of the chemistry and mechanics of developing cells and tissues. The nature of the effects of genes on details of morphology is likely to remain very largely a matter for speculation alone, until some at least of these gaps are filled. Here perhaps we may leave a volume which contains many important contributions to botanical thought.

W. H. Pearsall

HARVEY ON MOVEMENT IN ANIMALS

De Motu Locali Animalium, 1627

By William Harvey. Edited, translated and introduced by Dr. Gweneth Whitteridge. Pp. xii+163. (Cambridge: At the University Press, 1959. Published for the Royal College of Physicians.) 60*s*. net.

SIR RUSSELL BRAIN was president of the Royal College of Physicians when plans were being evolved to mark the Tercentenary of Harvey's death. *Inter alia*, proposals were made to the College Library Committee at one or more of its meetings that Dr. Gweneth Whitteridge, who is archivist to Harvey's Hospital of St. Bartholomew in the City of London, should first transcribe and later translate and duly introduce his "De motu locali animalium", which forms *ff*. 69–118 of the British Museum manuscript Sloane 486. This was written throughout in Harvey's own hand, and consists of his notes on the anatomy of muscles (*ff*. 1–68), followed by his "local movement in animals". A title, "Guilielmus Harveius de musculis, motu locali etc.", written on *f*. 1 of the double manuscript, may have been added by Sir Hans Sloane. Anyhow, Harvey's rough draft for his intended book on the local movement of animals was begun in 1627, was mentioned in *Cap. xvii* of his "Exercitatio anatomica de motu cordis et sanguinis in animalibus", 1628, and was added to on several occasions, but was never cast into final literary form. The notes, which came to light in the British Museum in the middle of the nineteenth century, have never before been transcribed, but they make clear the tenor of Harvey's projected work on muscle and, though containing no new experimental observations, show that his understanding of muscle and muscular contraction was sounder than that of his predecessors and even of some of his successors.

The work has been published for the Royal College of Physicians at the Cambridge University Press, and has as an illustration a photograph of *f*. 95 of the manuscript under ultra-violet light, as evidence that such treatment has not revealed the presence of any writing which was not previously visible. The edition is limited to 1,000 copies.

Its chief concern has been to provide a text which is readable. The English version of "De motu locali animalium" is not to be taken as a literal translation of the Latin text, for it was decided against following Harvey's Latin literally and reproducing his notes in note form in English. The alternative method adopted was to follow the arguments alluded to by Harvey and to expand his notes into complete sentences by reading the books which he was following, and as closely as possible completing the thoughts which he, for his own reference, needed only to note down in a few words. Inevitably, this method has led to a certain amount of interpretation which may or may not be correct. The English version is therefore offered merely as a suggested rendering.

Dr. Whitteridge thanks the Librarian and staff of the Library of the University of Edinburgh, which has on its shelves several of the actual editions of the works used by Harvey. She also thanks her husband, Prof. David Whitteridge, for his discussion of physiological problems and for his help in writing about the importance of Harvey's 1627 treatise in the history of muscle physiology. She further expresses gratitude to Dr. Lorenzo Minio-Paluello for his encouragement to one who, before this, knew nothing of the natural philosophy of Aristotle.

There can be no doubt that Dr. Whitteridge has done consummately well in transcribing Harvey's obscure handwriting, translating his Latin, and annotating his notes; as Sir Russell Brain says, she has earned the gratitude and admiration of students of Harvey all over the world, not least among them being the President and Fellows of the Royal College of Physicians of London, at whose request she undertook the work.

Though Harvey's notes, as already stated, contain no great discovery, they have "much of interest to the student of his mind. They show him, as always, gathering his illustrations from every kind of animal and even plant life, and in addition recalling clinical observations which must have impressed him".

K. J. FRANKLIN

RECONSTRUCTING THE PAST

Life and Death in the Bronze Age

An Archæologist's Field-Work. By Sir Cyril Fox. Pp. xxvii+193+49 plates. (London: Routledge and Kegan Paul, Ltd., 1959.) 45*s*. net.

THIRTY years ago prehistorians were content to collect the relics left by early man, and to accept the view that little, if any, knowledge of the life he lived could be obtained—they were satisfied to produce the skeleton, but fearful of attempting to clothe it with flesh and blood. It is true that occasionally—as, for example, when discussing palæolithic ceremonial burials or when the cave art was under consideration—it did seem permissible to talk about ritual and magic, but by and large it was felt to be dangerous to attempt to picture prehistoric man as a living individual, even with the help of such a kindred study as ethnology. How could one be certain that similar conditions in times very different must have produced a similar outlook on life ?

For some time past, however, a new approach to the study of prehistoric man has been developing, leading to just that ground where the earlier investigators feared to tread. This new approach can be dangerous and result in grave errors, but not when it is pursued by such a master of the subject as is Sir Cyril Fox. There is no doubt that if a brilliant investigator has lived with his work for much of a lifetime he develops a sixth sense which enables small circumstances to be noticed which fall severally into place until the intuition becomes a well-nigh demonstrable fact. This is what makes any work by Fox so fascinating. Any good excavator can dig up prehistoric relics in a highly satisfactory manner using all the modern techniques; but it takes a Fox so to live with the builders of, say, a megalith he is investigating as to see them at their work of building and performing the ritual for which the monument was raised—and then to convey all this to his readers. Fox has another advantage over many of his contemporaries in that he remains so young. Often the later, post-retirement, works of a savant make sad reading, but this is not at all the case with the book under review. There is a freshness about it all, even when mere descriptions of excavations are being given, which is stimulating and delightful.

The period under consideration covers the millennium 1700 B.C.–700 B.C., and the excavations in question were mostly situated in Wales and were mainly the author's own work. The volume is splendidly illustrated with plans, line blocks and half-tones. The chapters are arranged geographically—north Wales, west Wales, west and south Wales, the 'Food-vessel' phase in Britain, barrows in Glamorgan, etc. To start with there is a long introduction to the subject. Here the problems of the Bronze Age in general and barrows in particular are discussed and distributions considered. The stage is thus set for the account of a round barrow in Ysceifiog parish, North Wales, and at once we are made to see what must have happened there in the past.

Sites in the other geographical areas are treated in the same manner and we are thus given a vivid picture of how and in what order the processes connected with barrow-building took place—facts of construction that, having been appreciated, have sometimes "formed a basis for the recovery of an elaborate ceremonial". The various finds—pottery, tools, and the like—are, of course, carefully noted and their parallels elsewhere discussed. The Welsh monuments are not treated *in vacuo*; the importance of their geographical position *vis-à-vis* Ireland is stressed. "Life and Death in the Bronze Age" is well worth careful study not only for the many facts brought to light but also, as has been already said, for the vivid picture it affords of happenings which must have taken place in a millennium of the British Bronze Age.

M. C. Burkitt

THE EARLIEST GEOLOGICAL TREATISE

The Earliest Geological Treatise (1667)

By Nicolaus Steno (Niels Stensen). Translated from "Canis Carchariae Dissectum Caput", with Introduction and Notes by Dr. Axel Garboe. Pp. v+51+4 plates. (London: Macmillan and Co., Ltd., 1958.) 15*s*. net.

MODERN geology as an inductive science was born in Italy in the latter part of the seventeenth century, the most famous of the pioneers being Nicolaus Steno (Niels Stensen, 1638–86), "the learned Dane", who had settled in Florence. In 1669 appeared his "De solido intra solidum naturaliter contento dissertationis prodromus" (the Prodromus to a dissertation concerning solids naturally contained within solids), the importance of which was recognized by Henry Oldenburg, secretary of the Royal Society, who published a translation (London, 1671).

Steno was led to study rocks through the examination of a shark's head which had been sent to him for dissection, and his account, "Canis Carchariae dissectum caput", published two years before the Prodromus, contains an appendix, which Dr. Garboe has translated, in which some of the essential elements of the later work are set down.

Recognizing the 'tongue stones' (*glossopetrae*) found in the rocks of Malta to be in all respects similar to the teeth of living sharks, he argues cogently that these and other fossils are the remains of once living aquatic animals, and he combats the view then commonly held that these bodies had grown within the rocks. This appendix consists of eleven 'observations' of sedimentary rock features, followed by six 'conjectures' in which the origins of the sediments, their fossils, cross-cutting veins, and departure from horizontality are deduced.

It seems strange to the geologist of to-day that the reaching of such fundamental and seemingly obvious conclusions was so long delayed, but their apparent conflict with the teachings of an all-powerful Church not only hindered the recognition of the significance of the evidence but also made men wary of voicing their opinions.

Dr. Axel Garboe is to be thanked for this page-by-page translation, which makes available to the English-speaking world "the earliest geological treatise". As frontispiece there is a reproduction of the portrait of Steno as a young man (Uffizi Gallery, Florence); also there is a copy of the title page of the 1667 work and its figure of a shark's head and teeth.

L. Hawkes

PRINTED CIRCUITS

The Technology of Printed Circuits

The Foil Technique in Electronic Production. By Dr. Paul Eisler. Pp. x+405. (London: Heywood and Co., Ltd., 1959.) 60*s*. net.

PRINTED circuits have been developed in the past decade for use in equipment ranging from electronic computers to aircraft de-icing systems, and continue to replace manual wiring. In conjunction with component insertion machines they enable high rates of production to be attained with low labour and inspection costs, and a greater uniformity of product than was possible by previous methods of wiring.

The book gives ample evidence of the author's position as a leading contributor to the technology of printed circuits, and the inventor of the printed foil technique now in general use.

The first two chapters describe early attempts at printed circuit production, and alternative methods such as spraying, stencilling, die-stamping and plating.

Chapters 3–8 contain a full account of the large-scale manufacture of printed circuit boards, including the photography of the master drawing, the preparation of the raw material, the printing processes, and etching and cleaning. Chapter 9 gives details of the subsequent operations such as the deposition of protective coatings, soldering and encapsulation.

Chapter 10 contains an excellent description of the small-scale production of printed circuits, and the laboratory apparatus required.

The following three chapters deal with the design of printed circuits, the selection of foil and insulating board, the choice of components, automatic assembly and fault finding.

The final chapters describe methods of reducing the weight and size of electronic equipment, the use of printed components, and the application of printed circuits to microwave systems and electronic devices. An excellent bibliography is included.

The wealth of practical detail given in the early chapters will be invaluable to those engaged in the manufacture and design of printed circuit assemblies, but the general reader would welcome more information about the use of printed circuits in various branches of the electrical industry, and their influence on system design, mechanical lay-out, and maintenance procedure.

However, this is the most comprehensive treatment of the subject generally available, and it is clearly destined to become the standard work of reference on printed circuit technology.

J. C. Cluley

BICENTENARY OF THE ROYAL BOTANIC GARDENS, KEW

By DR. W. B. TURRILL, O.B.E., F.R.S.
Formerly Keeper of the Herbarium and Library

THE choice of 1959 as the bicentenary of the Royal Botanic Gardens, Kew, is approximately a correct one so far as the present Gardens are concerned. There is at least one reference to a garden at Kew belonging to the Rev. William Turner (c. 1510–68), who has been termed 'the father of English botany'. Sir Henry Capel (?–1696) was also a notable cultivator of plants, but mainly from the horticultural rather than the botanical point of view. His property at Kew descended to a grand-niece, Lady Elizabeth Capel, who married Mr. Samuel Molyneux, a politician and secretary to the Prince of Wales (later George II). On the death of Molyneux's widow in 1730, the then Prince of Wales, Frederick Louis, obtained a lease of Kew House and laid out the grounds afresh. Frederick married the Princess Augusta of Saxe-Gotha in 1736 and died in 1751. The Princess Augusta, then Dowager Princess of Wales, continued to live at Kew, and about 1759, with the help and advice of John Stuart, third Earl of Bute (1713–92), who was sincerely interested in botany, laid out about nine acres of the grounds of Kew House as a botanic garden and appointed the architect, Sir William Chambers (1726–96), to embellish the garden and the adjacent pleasure grounds. Many of the buildings erected by Chambers have now disappeared, but several remain, of which the most noteworthy are the Orangery (1760–61) and the Pagoda (1761–62).

Perhaps the most important happening, from the practical point of view, of this period was the appointment in 1759 of William Aiton (1731–93) as superintendent of the botanic garden. Aiton was a botanist as well as a gardener, and in 1789 published his "Hortus Kewensis", or a "Catalogue of the Plants Cultivated in the Royal Botanic Garden, Kew". This work, in three volumes, includes 5,500 species which are named, often described, and classified according to the Linnean system.

Aiton, at first, had under his charge only the relatively small botanic garden of the Princess Augusta; but his responsibilities were increased more or less gradually, and in 1784 he took over the entire management of both the Royal Gardens of Kew and Richmond. William Aiton died in 1793 and was succeeded by his eldest son, William Townsend Aiton (1766–1849), who published a second edition of the "Hortus Kewensis" in five volumes.

While the Aitons were head gardeners, superintendents, or what would now be called curators of Kew, it was first to the Earl of Bute and later to Sir Joseph Banks that the development of Kew on the purely botanical side was very largely due. The former was unofficial director of Kew under the Princess Augusta. The deaths of his father and grandfather (George II) brought the Kew and adjacent Richmond properties into the ownership of George III, and in 1765 the King obtained powers from Parliament to close the public right of way, known as Love Lane, which separated the two "Gardens". Though the closure was not completed for some years, it was from this fusion of the gardens (botanic and pleasure) of Kew House and part of those of Richmond Lodge that the present title of Royal Botanic Gardens (in the plural) originated. George III, Queen Charlotte, and their family (fifteen sons and daughters) spent much time at Kew, where the King delighted to play the part of 'Farmer George'.

When the Princess Augusta died in 1772 her property came immediately and fully into the possession of George III, who replaced the Earl of Bute by Sir Joseph Banks as adviser on the botanical developments at Kew. Banks planned to grow species of plants from all parts of the world in the botanic garden. He sent trained collectors to many countries overseas, bombarded ministers and government officials with letters of instruction, sometimes almost of command, and gave freely of his time, energy, and money to this end. It is said that about seven thousand plants from abroad new to cultivation in England were thus introduced to Kew during the reign of George III. Among the 'Kew collectors' of this period were Francis Masson (1741–1806), who collected in South Africa, the West Indies and North America; David Nelson (died 1789), who visited Australia, South Africa and Timor; A. P. Hove, who was in India during 1787–89; Peter Good (died 1803), who sent plants from India and Australia; George Caley (died 1829), who went to Australia; William Ker (died 1841), an early collector in China; the brilliant botanist, Allan Cunningham (1791–1839), who collected widely in Brazil, South Africa, Australia and New Zealand; James Bowie (died 1869), who sent material from Brazil and South Africa; and David Lockhart (died 1846), who went to the Congo and, later, to Trinidad. Another collector who, through Sir Joseph Banks, made important contributions to the botanical development of Kew was Archibald Menzies (1754–1842), who was surgeon and botanist to Captain George Vancouver (1758–98) in his voyage of survey (1791–95) and sent plants from Australia, South America and western North America. He introduced the monkey puzzle (*Araucaria araucana*) from Chile to Kew and was the discoverer of the redwood (*Sequoia sempervirens*) in California.

George III and Sir Joseph Banks both died in 1820, and Kew passed into a period of relative decline. No more collectors were sent out from Kew, though seeds and plants continued to be received from overseas. That the Gardens did not die as a botanical institution was largely due to John Smith (1798–1888), who was made W. T. Aiton's chief assistant in 1826 and later, under Sir William Hooker, became curator. In January 1838 the Treasury appointed a committee "to inquire into the management, etc., of the Royal Gardens". This committee consisted of Dr. John Lindley, a renowned botanist and author of "The Vegetable Kingdom", Mr. (later Sir) Joseph Paxton, and a Mr. Wilson, gardener to the Earl of Surrey. The resulting report described the collections, then at Kew, their condition, the state of the greenhouses, etc., and was extremely critical, though the report was itself criticized by John Smith in his "Records". However, the report on the constructive side pointed out strongly the need for a well-managed and well-equipped botanic garden in Great Britain. It was presented to Parlia-

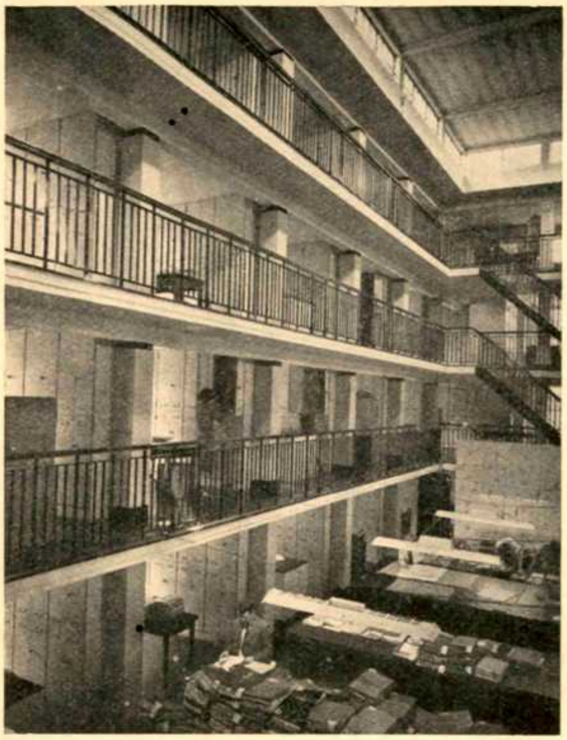


Fig. 1. Part of the Herbarium, Royal Botanic Gardens, Kew

ment on May 12, 1840, and as a result the control of Kew was transferred from the Lord Steward to the Commissioners of Woods and Forests, that is, from being the personal property of the Crown to the nation. Sir William Jackson Hooker, then regius professor of botany in the University of Glasgow, was appointed director in March 1841.

Kew as we know it to-day is very largely the creation of Sir William Hooker. Apart from being a first-class botanist, he was an organizer and administrator of the first rank. When he became the first director of Kew officially appointed by the Government, the garden area in his charge was only about 15 acres, and this was divided by brick walls which he speedily had pulled down. When he died, in 1865, six weeks past his eightieth birthday, Kew Gardens extended over 250 acres. Such figures, however, are only superficial indications of what Sir William did for Kew. New plants were received from many sources, a large part of the ground was laid out afresh, the Palm House was built between 1844 and 1848, the first Museum of Economic Botany was opened to the public in 1848, the Herbarium and Library were commenced in 1853, the Lake was completed in 1856, the first flagstaff successfully erected was presented in 1861, and the Temperate House was completed in 1862. Sir William continued his botanical and editorial activities, many of which had been started in Glasgow, after his appointment as director of Kew, and he encouraged botanical research by his staff and by visitors.

Sir William's only surviving son, Joseph Dalton Hooker (knighted in 1877), had been assistant director during 1855–65 and was appointed director in immediate succession to his father. He was born, as the second son, in 1817 and was educated in Glasgow. After taking his M.D., he was appointed assistant surgeon in the Royal Navy and was gazetted to the *Erebus* which, with the *Terror*, under the command of Captain (later Sir) James Ross, visited many parts of the southern hemisphere. J. D. Hooker's large collections were later worked out by him and published in a series of important volumes dealing with the taxonomy and phytogeography of the countries explored. From late 1847 until early 1851 he was in India and for three entire years explored and collected especially in Sikkim, eastern Nepal, and the Khasia Hills. His interest in Indian botany, which culminated in the preparation and publication of "The Flora of British India" (seven volumes, 1872–97), remained with him all his life. After his appointment as director of Kew, J. D. Hooker undertook two more botanical journeys, one to Morocco in 1871 and one to western North America in 1877. The most important taxonomic work was the "Genera Plantarum" (1862–83), written in collaboration with George Bentham and containing descriptions in Latin of all the then known families and genera of seed-bearing plants. These descriptions have, as a whole, never been excelled, and the volumes are still constantly used by taxonomists. Besides his own researches, J. D. Hooker encouraged much and diverse botanical investigation at Kew, particularly in taxonomy, plant geography, and economic botany. He made numerous improvements in the Gardens. Thus, he planted the Pinetum, brought the Berberis Dell to its present condition, created the Rock Garden, planted the Holly Walk, and improved avenues and vistas. The T-range was erected in 1868–69, the Jodrell Laboratory was built in 1876, a new wing was completed for the Herbarium in 1877, a wing added to Museum I in 1881, and the North Gallery opened to the public in 1882. After his retirement from the directorship in 1885, Sir Joseph Hooker lived at Sunningdale in Berkshire and continued to edit the "Icones Plantarum" until the end of 1889 and the *Botanical Magazine* until 1902 and for two years more with assistance. He completed the "Flora of British India", and during the final years of his long life continued researches in the genus *Impatiens*, results of which were published up to the year of his death, 1911. He was buried, with his father, in the family vault in St. Anne's Churchyard, Kew.

The history of Kew during 1841–85 is almost synonymous with the biographies, during that period, of the two Hookers, father and son. It gives some idea of their tremendous activities to record that in

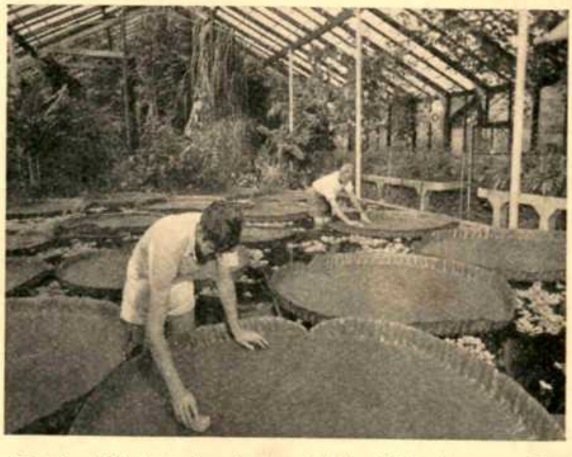


Fig. 2. *Victoria regia*, giant water-lily of the Amazon. The leaves attain a diameter of up to 6 ft.

the Kew Library there are 76 volumes (many large) of Hookerian correspondence. Administration had its difficulties, and the famous controversy in 1872 between the director and his official superior, the First Commissioner of Works, A. S. Ayrton, led to debates in both Houses of Parliament, the publication of a 'bluebook', and finally the placing of the authority of the director of Kew on a firmer basis.

J. D. Hooker was succeeded in the directorship by his son-in-law, William Turner Thiselton Dyer (the last two names became hyphened about 1891). Dyer was particularly keen on making Kew the botanical centre of the British Empire, especially as regards plant taxonomy and economic botany, and he did much in this direction by stimulating the preparation of Colonial floras. A new wing of the Herbarium was built in 1902, and the *Kew Bulletin of Miscellaneous Information* (afterwards the *Kew Bulletin*) was started in 1887. The original "Index Kewensis" was published in 1895. Improvements were made in the Gardens, and houses for alpine plants, filmy ferns and pitcher plants were erected. The Queen's Cottage Grounds were given in 1898 by Queen Victoria to Kew to commemorate her Diamond Jubilee, and Cambridge Cottage and its walled garden were added in 1904. On April 1, 1903, the Royal Botanic Gardens, Kew, were transferred from the Office of Works to the Board of Agriculture and Fisheries (now the Ministry of Agriculture, Fisheries and Food).

Thiselton-Dyer resigned in December 1905 and was succeeded by Lieut.-Col. David Prain, who steadily developed the scientific activities of Kew until 1922, in spite of setbacks during the First World War. Dr. A. W. (later Sir Arthur) Hill was director from 1922 until his tragic death in a riding accident in 1941. After a short interval, Prof. E. J. (later Sir Edward) Salisbury was appointed to the directorship and retired in 1956, and the present director is Dr. G. Taylor, formerly keeper of the Department of Botany, British Museum (Natural History). During the past fifty years, additions to Kew include a fine new wing to the Herbarium (built in 1931), enlargements to the Rock Gardens, the Sherman-Hoyt House for Succulents, a Chalk Garden, a Clematis Wall, a modern Australian House, and new accommodation for the Orchid Collection. Many of the greenhouses have been renovated or reconstructed since the Second World War, notably the Palm House. The old Orangery, designed by Sir William Chambers and erected in 1760–61 and long used as a museum for timber exhibits, etc., is being converted to serve again its original purpose.

Since 1841 the Royal Botanic Gardens, Kew, have been a government institution serving an international function—the advancement of botanical science. From the nature of botany, certain divisions of the subject can only be studied adequately at a large central institution, and it is these that are the special concern of Kew. In particular, the three branches of plant taxonomy, phytogeography, and economic botany require large collections of specimens, a first-class library and facilities for wide contacts overseas. Kew provides these conditions probably more adequately than any other institution in the world, both to members of the staff and to very many students from all countries who visit Kew for longer or shorter periods. In addition, a great deal of assistance is given to correspondents in answering a very large variety of questions, in providing material for research, and in loaning specimens to recognized botanical institutions. The work of Kew is not limited to the three branches of botany mentioned above, but it is even more essential to record that these branches themselves are considered at Kew along modern lines to include or to have contact with most of the specialized subdivisions of botany that are dealt with in other institutions. Of the large collections at Kew that are available for research one may mention the living plants in the Gardens, with more than 45,000 species, the Herbarium of dried specimens exceeding 6,000,000 sheets including more than 200,000 types, the sets of microscope slides at the Jodrell Laboratory, and the extensive series of samples of economic products (timbers, fibres, foods, drugs, etc.) in the museums.

The continued contribution of Kew to botanical research may be briefly indicated by reference to publications. The long series of floras produced at Kew include the "Flora Australiensis", the "Flora of British India", the "Flora of Tropical Africa", the "Flora Capensis", the "Flora of West Tropical Africa" (now being revised), and many smaller works. In course of preparation, and in part publication, are the "Flora of Tropical East Africa", the "Flora of Cyprus", the "Flora of Iraq" and (in collaboration) the "Flora Zambesiaca". Assistance is also being given in the preparation of the "Flora of Trinidad and Tobago" and the "Flora Malesiana". The *Kew Bulletin* is now published with three parts to an annual volume and contains papers, mostly by members of the staff, on a variety of botanical subjects. The "Index Kewensis", one of the most useful works to systematists concerned with vascular plants, is compiled at Kew and supplements are now published quinquennially. The "Icones Plantarum" consists of black-and-white figures, with descriptions and other information, of plants preserved in the Kew Herbarium, and is published by the Bentham–Moxon trustees in parts at intervals. The *Botanical Magazine*, the oldest botanical and one of the oldest scientific publications still continuing, was commenced in 1787 and has been connected with Kew for more than a century. It has coloured figures prepared from living plants grown at Kew or in other British gardens with accompanying text giving a full descriptive and general botanical account of the plants depicted. It is prepared at Kew and published by the Royal Horticultural Society as a biennial volume of four parts. In addition to the floras and periodicals enumerated, members of the Kew staff contribute scientific papers to many scientific journals and societies and have published various independent books on a wide range of subjects including taxonomy, plant anatomy, phytogeography, economic products, ecology, and genetics.

In this brief sketch of the history and functions of Kew emphasis has been placed on the botanical activities of the institution. The educational and recreational value to the public are also very considerable. The Gardens are interesting and beautiful at all seasons of the year, above all in the months of May and June. In 1958, a 'bad weather' year, the number of visitors passing through the turnstiles was 946,499, and though many of these came for a 'day's outing', a high proportion gained knowledge concerning the wealth of form, colour and behaviour of a great range of plant life and of the use of trees, shrubs, and herbs in man's economic and æsthetic life. Kew's contribution to the welfare of the nation, the Commonwealth, and the world cannot be precisely measured in monetary or any other terms, but it is certainly very great.

THE MECHANISM OF DETERGENCE

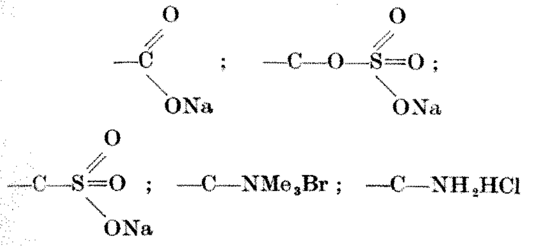
By Dr. A. S. C. LAWRENCE
Department of Chemistry, University of Sheffield

FOR nearly forty years since the discovery of orientated monomolecular films, detergent action has been described in terms of adsorption, wetting angles and reduction of surface free energy. Substrate and dirt have been regarded as inert non-polar surfaces on to which the soap is adsorbed with the hydrocarbon chain inwards and the polar group outwards to give wetting by water. As generalizations, the first is dubious and the second untrue. This general theory has no place for specificities of soaps for soils or substrates, nor can it explain the nature of the actual detachment and breaking up of dirts of sticky consistency and strongly adherent character. Indeed, some writers have been careful to say that there is no justification for saying that detergence is a spontaneous process. Nevertheless there is in the detergence of polar dirt a spontaneous process of penetration of soap and water into the dirt, followed by peptization. This process has nothing to do with surface forces, but results from cryoscopic forces and diffusion processes in the ternary soap/water/polar dirt system. This new picture of the mechanism of detergence arises from the following considerations.

It is now known that a large number of organic substances, especially fatty ones, are soluble in aqueous soap solution even though insoluble in water, and that substances partially miscible in water have their mutual solubilities greatly increased by addition of soap. By 'soap' I mean any substance which has the properties of soap; that is, a substance which in aqueous solution is surface active, froths, emulsifies oils and has detergent action: a definition which includes the substances variously described as synthetic detergents, syndets, surface-active agents, surfactants and even, in the horrible advertising jargon, 'soapless soaps'. Those most studied are of the type:

$$\underset{R_1}{\sim\sim\sim\sim\sim\sim\sim\sim}(S)$$

where R_1 is a saturated hydrocarbon chain of 12, 16 or 18 carbon atoms, and the oleyl soaps, which have a C_{18} chain with a double bond in the 9 : 10 position, and the *cis* configuration, which gives them solubility corresponding more nearly with the C_{12} saturated chain than the C_{18} chain. S represents:



$$-\overset{\overset{O}{/\!/}}{C}\!\underset{\underset{ONa}{\diagdown}}{} \;;\quad -C-O-\overset{\overset{O}{/\!/}}{S}\!=\!O\underset{\underset{ONa}{\diagdown}}{} \;;$$

$$-C-\overset{\overset{O}{/\!/}}{S}\!=\!O\underset{\underset{ONa}{\diagdown}}{} \;;\quad -C-NMe_3Br\;;\quad -C-NH_2HCl$$

I am not concerned now with non-ionic soaps, where the picture is more confused. The organic substances which we have studied most thoroughly are the aliphatic acids, alcohols, and amines, which may be written generally as:

$$\underset{R_2}{\sim\sim\sim\sim\sim\sim\sim\sim}(A)$$

A benzene ring can be included in the R_2 chain and more complex substances such as cholesterol show similar solubility effects. These are all substances of the type named by Winsor 'amphiphilic'[1]; that is, substances containing both a polar water-soluble group and a water-insoluble group of size sufficient to confer hydrophobic properties—a structure which ensures that the two parts of the molecule always have opposed solubility tendencies. Winsor includes the soaps in the amphiphilic class, but I prefer to keep them out of it and call them soaps.

Ternary Soap/Water/Amphiphile Systems

At first sight, the changes observed when an amphiphile is added to aqueous soap solutions of various concentrations seem quite irrational, and phase analysis appears to be impossible because of the very high viscosities encountered. Once, however, the presence of a ternary liquid crystalline phase existing over a wide range of concentrations was established[2], study of phase equilibria became possible, and the full triangular diagrams have shown a remarkable consistency independent of the nature and charge of S and A, or of R_1 and R_2 provided R_2 contains five or more normal carbon atoms (Fig. 1)[3-5]. The diagram consists essentially of five areas (Fig. 1); at the top, at high concentrations of soap, solid soap exists; at the bottom, below about 10 per cent soap, there are two liquids, sometimes as separate phases or, with higher values of R_2, as a system in which the aqueous isotropic phase is enclosed in membranes of liquid-crystalline phase and which defy mechanical separation. This is not an emulsion although it resembles one to casual visual inspection. At the water-rich corner, L_1 is isotropic solution; this is the region of McBain's 'solubilization'. At the corner rich in organic component another isotropic liquid, L_2, exists; this is not formed merely by turning the micelles in L_1

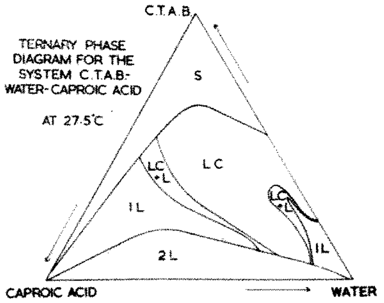


Fig. 1. Typical phase diagram for soap/water/amphiphile system. The diagram is for hexadecyltrimethylammonium bromide, water and hexanoic (caproic) acid at 27·5° C.

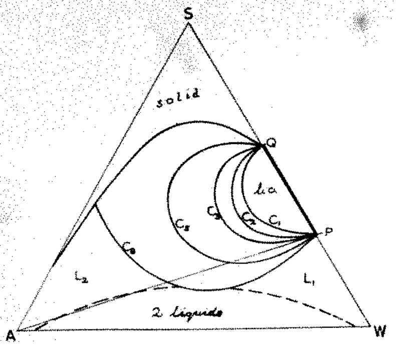


Fig. 2. Simplified diagram of the effect of chain-length of amphiphile (R_2) upon the phase boundaries of the ternary liquid-crystalline phase

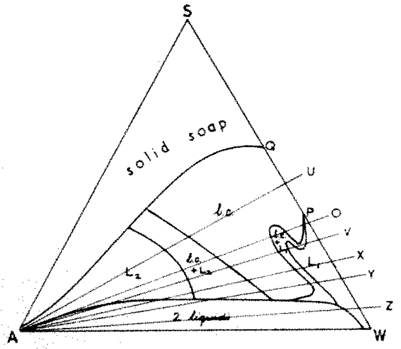


Fig. 3. Phase diagram for the system: sodium dodecyl sulphate/water/hexanoic (caproic) acid. Tie lines are shown to indicate the different sequences of changes when caproic acid is added to different initial concentrations of soap in water at 25° C.

inside out; they are reversed so as to become lipophilic in L_2 but, as they contain water, they are emulsions of truly colloidal dispersion[6], as opposed to the classical emulsions the dimensions of which place them far outside the range of true colloids. L_2 is the region of formation of the commercial 'soluble oils' when hydrocarbon is added as a fourth component. *LC* is the 100 per cent (smectic) liquid-crystalline phase flanked on either side by an area of $LC + L_1$ or L_2.

When R_2 is a 1, 2 or 3 carbon-atom chain or if the amphiphile is phenol or cresol, no two-liquid area occurs, L_1 and L_2 become continuous and extend to the base of the triangle. The liquid-crystalline (*l.c.*) phase, however, still exists as shown in Fig. 2. From this and from Fig. 1 it is clear that the *l.c.* area has, as base on the soap–water side of the triangle, the range of concentrations, *PQ*, over which the binary soap/water system is liquid-crystalline. This has been shown most clearly by Dervichian[7] in his potassium hexoate/water/methanol system; it is also clear why, starting from isotropic soap solutions, and adding the organic amphiphile, we do not observe liquid-crystalline phase when R_2 is a chain of less than five carbon atoms; the ternary liquid-crystalline phase exists but it is necessary to start with a soap solution which is already in the binary liquid-crystalline phase (tie line *AP*, Fig. 2 and *AU* in Fig. 3). If in Figs. 1, 2 and 3 we choose a concentration of soap in water and add amphiphile to it, we travel along a tie-line from that initial concentration to the 100 per cent amphiphile corner; the great variety of phase changes observed for initial soap concentrations of *U*, *V*, *X*, *Y* and *Z* are indicated in Fig. 3, which represents the phase diagram for sodium dodecyl-sulphate with caproic acid (amphiphile) and water. We see that we shall get different changes starting from concentration *V* of hexadecyltrimethylammonium bromide and of sodium dodecyl sulphate in Figs. 1 and 3. Again, if we wish to make a soluble-oil type such that no separation into two liquid phases occurs, then the minimum soap concentration is given by *AO*, the tie line from *A* tangential to the top of the two-liquid phase area.

This picture applies to all ionic soaps and amphiphiles regardless of the nature of the radicals *A* and *S* or of the sign of their charges. We have made a number of fatty alcohol/ethylene oxide-chain soaps which are interesting in so far as their solubility depends upon hydrogen bonding between the ethylene oxide chain and water. The aqueous solutions show a lower consolute temperature; that is, the soap and water separate into two liquid layers when the aqueous solution is heated. Addition of amphiphiles will lead to competition for hydrogen bonding and the case is different from that of ionic soaps. I suspect also that all these soaps are in fact true soaps solubilizing some of the lower water-insoluble polymers containing one, two or three ethylene oxide chains; the stepwise addition of ethylene oxide to form the polymer chain ensures that with an average number of, say, 6 ethylene oxide chains there must be some with more or some with fewer chains; the latter, together with any unreacted *R*OH, will therefore constitute amphiphiles already present in the soap solution, and extreme caution is necessary in interpreting the results of further deliberate addition of other amphiphiles.

Temperature Effects

With the higher homologues of the aliphatic amphiphiles, a lower temperature limit to the existence of the ternary liquid-crystalline phase is set by the point where the amphiphile crystallizes out; when this is present in excess, it freezes out at 2–3 deg. C. below its melting point. At more nearly equal ratios of soap and amphiphile, however, there is a large depression of freezing point such that the

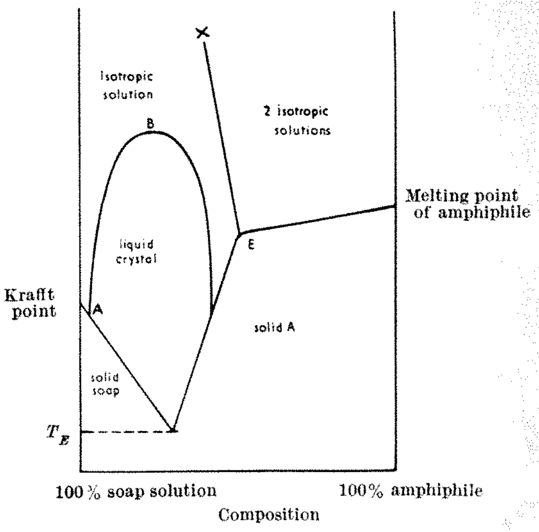
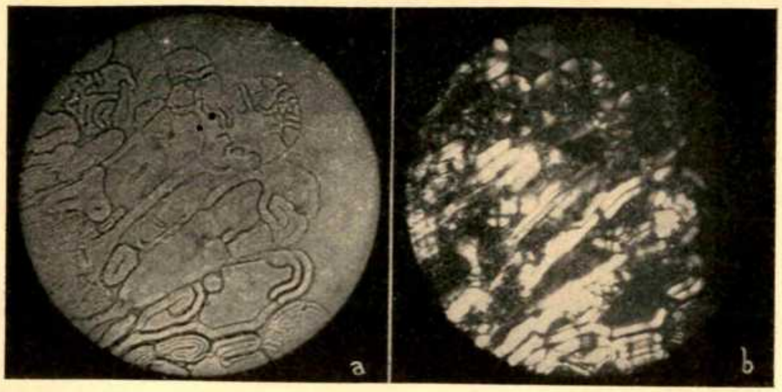


Fig. 4. Tentative temperature – composition diagram for soap/water/amphiphile systems for any selected soap–water concentration from the minimum required to avoid the two-liquid layer region up to the maximum at which the soap solution becomes liquid crystalline



Nicols parallel (×50) Nicols crossed

Fig. 5. Myeline figures formed by penetration of water into an equimolecular mixture of sodium laurate and oleic acid; after about 10 min. at 20° C.

liquid-crystalline phase is stable at room temperature. Fig. 4 shows the temperature – composition diagram for such systems, treating them as binary mixtures with soap and water as one component and the amphiphile as the other; the Krafft point of the aqueous solution is taken as a melting point, while the other melting point is, of course, the orthodox one. It applies to all soap/water ratios between the minimum of about 10 per cent required to prevent formation of the lower two-liquid area and the upper limit at which the binary soap/water system becomes liquid crystalline. It will be seen that this is only a partial limitation involving the movement of the left-hand rising boundary of the *l.c.* phase from *A* to the $(S + W)$ axis; the low-temperature eutectic part of the diagram below the Krafft point being unaffected.

If the lower axis of the graph represents room temperature, then on the left we have solid soap plus solution; on the right, solid amphiphile plus solution; and in the centre ternary liquid-crystalline phase: this is found even with cholesterol as amphiphile which, in spite of its high melting point (147° C.), persists at 0° C. The upper temperature limit of the liquid-crystalline phase is usually above 100° C. The other cases in which either the melting point of the amphiphile or the Krafft point is below 0° C. have been described elsewhere[3]; also the case where both are below 0° C. and the first solid to separate out is ice.

Penetration Experiments

Fig. 4 suggests that the ternary liquid-crystalline phase should form spontaneously at room temperature by mixing the components. This can be shown to occur in two ways, both being observed most conveniently by the polarizing microscope. First, by placing a very small piece of soap plus amphiphile, as solid (or paste if the latter component is liquid), pressing a cover-glass down gently and then flooding with water. After 5–10 min., a crop of myelinic tubular forms is seen under a magnification of 50; they are best seen with the nicols parallel (Fig. 5*a*), although with crossed nicols the myelines are seen to be strongly birefringent close to the original material and becoming less and less so as they become more elongated. Finally, the outer part breaks up by dissolving to form an isotropic solution, L_1 (Fig. 5*b*).

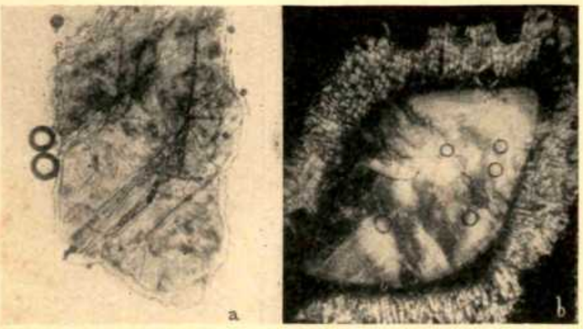


Fig. 6. Penetration of 15 per cent sodium dodecyl sulphate solution into solid stearic acid at 50° C.; (*a*) initial membrane in white light, and (*b*) after 6 min. in polarized light (× 20)

The second way is by immersing the solid amphiphile in soap solution; here also spontaneous formation of the ternary liquid-crystalline phase occurs but with two differences: the tubular myeline-like protuberances shown in Fig. 6 are sausages of liquid crystal and not tubular like the true myelines which have solution inside, and are elongated because the membrane containing them is a smectic liquid crystal with the axes of the long-chain molecules normal to the axis of the myeline so that extension can therefore take place only in a telescopic manner.

The second difference is that there is a sharply defined minimum temperature above which penetration of the soap solution into the solid amphiphile occurs (Fig. 7). Below this temperature (T_{pen}) only very slow formation of isotropic solution L_1 is

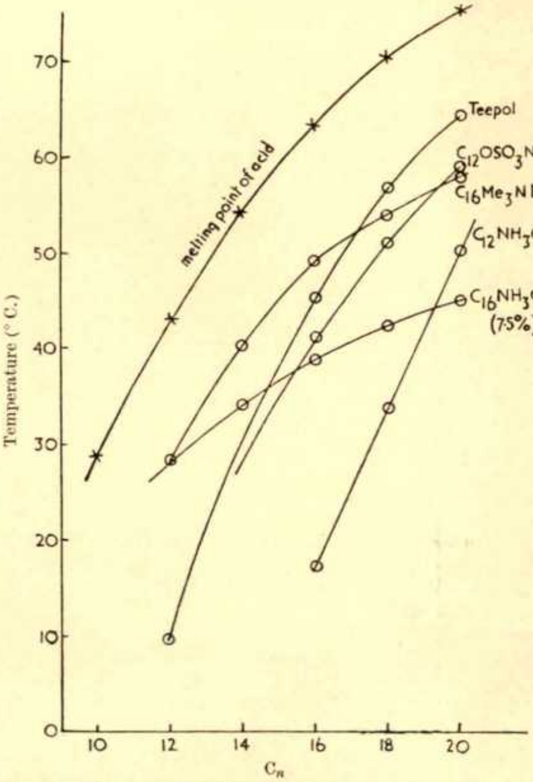


Fig. 7. Variation of temperature of penetration with chain-length for homologous fatty acids

observed. T_{pen} is several degrees below the melting point of the pure fatty amphiphile, and in the case of the eutectic curve of stearic and palmitic acids falls on a eutectoid curve with its minimum at the same composition but at a lower temperature (Fig. 8). Clearly T_{pen} should be identical with T_E, the eutectic temperature in Fig. 4. It is of interest in connexion with the ease of this penetration that the liquid crystalline growths are around the periphery of the crystal where polar groups are accessible and not on the large surfaces of the plates which are the terminal methyl groups.

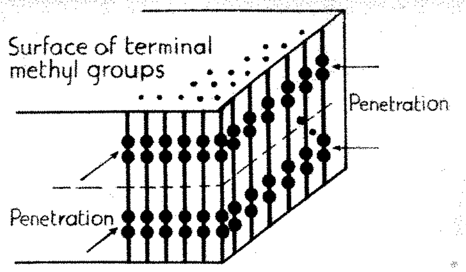


Fig. 9. Plate-shaped crystal of fatty amphiphile showing that the polar groups are accessible at the edges but not on the large flat faces of the plates

Detergence

It then occurred to me that these fatty amphiphiles are dirt—polar dirt it is true, but most dirt is partially polar—and that Fig. 7 is a picture of the spontaneous action of a detergent penetrating and peptizing dirt; that the triangular diagrams are soap/water/dirt phase diagrams and that Fig. 4 is the diagram of the temperature changes involved in detergence. Myeline formation has been reported in detergence by Stevenson[8] and also by Harker[9].

It may be objected that the process described requires a concentration of soap much larger than that normally used in detergence, but the objection is not valid because there will be a close-packed adsorbed monolayer of soap at the solution–dirt interface. At the point of attack the soap will always be a condensed phase and the interaction is of zero order with respect to the bulk concentration of soap. In fact, penetration occurs with solutions as dilute as 0·1 per cent.

Any line drawn from the solid stearic acid (shown in Fig. 6*b*) out into the isotropic solution is a tie line on the triangular phase diagram (perhaps not on a linear scale) from the 100 per cent amphiphile corner to the appropriate soap concentration; for example, *AO* in Fig. 3. We pass from solid amphiphile through fluid L_2 solution, very viscous *l.c.* into fluid L_1 solution; the dark isotropic ring around the stearic acid is the L_2 solution and, if the cover glass is disturbed, the *l.c.* phase is broken up, and floats away. Soap diffuses in again and builds up more *l.c.* and reduces the rate of diffusion of soap inwards. The gelatinous *l.c.* membrane is always separated from the 'dirt' by fluid L_2 phase; this is the reason why all washing requires agitation.

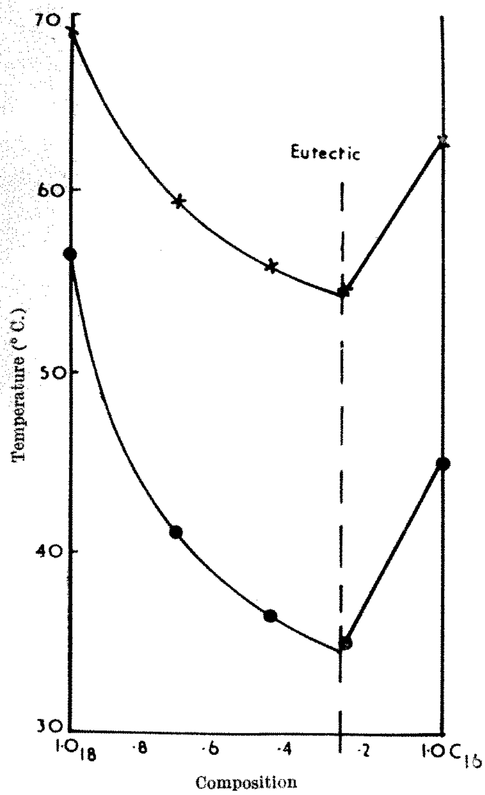


Fig. 8. T_{pen} for eutectic mixtures of stearic and palmitic acids; soap solution is 15 per cent sodium dodecyl sulphate

As described, fatty acids and alkanols are readily penetrated at temperatures greater than T_{pen}. Glycerin monolaurate was also penetrated but not the dilaurate. Addition of fatty acid or alcohol to 'Nujol' and paraffin wax showed that penetration in the former required a minimum concentration of about 10 per cent, whereas the wax needed at least 20 per cent.

An account has been presented of a mechanism of the process of detergence in terms of cryoscopic forces; the existing theory in terms of surface tension and free surface energy has always ignored this fundamental process. Wetting-angle phenomena are not affected by the new picture. Two outstanding problems, that of the very large temperature coefficient of efficiency of detergence and the rather mysterious one of 'redeposition', may well become explicable; the first as an increased rate of diffusion and the second by the fact that rinsing is a dilution so that we drop almost to the bottom of the ternary diagram into the two-liquid area, and, in this, the soap is in the organic phase: that is to say, the dirt is taking the soap out of the water.

The mechanism postulated here suggests that detergence is not brought about by free surface energy phenomena but by cryoscopic forces only. Ternary eutectic formation is by the water and the two water-soluble groups; the liquid crystalline properties result from the close-packing of the water-insoluble hydrocarbon 'tails' attached to the polar groups of soap and fatty soil.

I am indebted to Dr. T. Malkin for pure specimens of glycerin monolaurate and dilaurate.

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DEVELOPMENTS IN PHOTOELASTICITY

COMMEMORATION AT UNIVERSITY COLLEGE, LONDON

A JUBILEE commemorative exhibition of photoelasticity has been held in University College, London. With a lecture delivered on April 15 by Colonel H. T. Jessop, special lecturer in photoelasticity in the College and sometime research assistant to Prof. L. N. G. Filon, it recorded the progress made in this method of stress exploration in the fifty years since its two most formidable protagonists, Profs. Coker and Filon, began their uneasy but extremely profitable partnership ; E. G. Coker was the Kennedy professor of engineering and L. N. G. Filon was the Goldsmid professor of applied mathematics in the College.

In 1909 Prof. Filon had been working for some years on the optical phenomenon of stress-induced birefringence, which had remained a laboratory curiosity since its original discovery by Brewster in 1816. While an undergraduate at University College, he had become interested, too, in the mathematical theory of elasticity as a result of his contact with Karl Pearson.

By 1909 Prof. Coker had also been attracted by the subject and his interest was that of a mathematically uninhibited engineer. He wanted to know the stresses in bodies for the purposes of design studies. He was introduced to photoelasticity by Silvanus Thompson and, in a four-year period of collaboration, these two men proposed a series of stress investigations using celluloid models of structures having engineering significance.

Coker seems to have been the first to realize the practical engineering significance of stress-induced birefringence, and his proposals precede similar work of Mesnager (who used glass) by three years. Coker's use of celluloid models was largely intuitive, and Filon pointed out the many theoretical questions that it begged. This brought the two men together, though no details are available of the first meeting in 1909. They clearly had very different approaches to the subject ; even so, their subsequent collaboration lasted until Coker's retirement twenty-seven years later. Furthermore, the text-book which bears their names has no equal, and is, for those interested in photoelasticity, what Love's treatise has been for elasticians.

The Exhibition of Apparatus

The early exhibits show the differing interests of these two pioneers. Filon's experiments and apparatus illustrate his concern with the optical behaviour of materials, and in particular glass, under simple and calculable states of stress. Coker's apparatus shows how he wanted the practical answers that could be obtained from each experiment, and he seems to have taken it as axiomatic that the elastic stresses—and in particular the maximum values of stress—were the significant quantities. Coker concerned himself with the purely two-dimensional problem of photoelasticity with three unknown quantities at each point. For his purposes, the directions of the principal stresses were obtained from isoclinics in a plane polariscope, the difference between the two principal stresses was deduced from the isochromatics in a circular polariscope, and their sum was found by the measurement of lateral strains. To this limited extent Coker could have claimed that he had completely 'solved' the problem of two-dimensional photoelasticity—indeed, the claim has often been made for him.

Filon seems to have distrusted the lateral strain measurements, although he verified their validity for a state of 'generalized plane stress'. He relied instead on the differential equation of equilibrium to give him the extra information which permitted the principal stresses to be separated. But for Filon's approach, the measurements which could be taken were not sufficiently accurate to justify calculation of their derivatives. This led him to consideration of stress trajectories which gave a curvilinear coordinate system, from which the so-called Lamé–Maxwell equations could be obtained. The errors of calculation were then mainly included in a single estimate of a radius of curvature.

Only a few pieces of Filon's apparatus survived the bombing in the Second World War. His first experiment on a glass beam in bending still exists, but the rest of the original apparatus has been lost. Two of his early experiments on dispersion and a calibration experiment on glass have been reassembled by Colonel Jessop, who was Filon's research assistant when the experiments were performed. Many of Coker's ingenious loading rigs and other pieces of his apparatus still exist. They illustrate his interest in stressed bodies of complex shape which, while they are far removed from mathematical abstraction, are common in engineering practice.

Not only were 'museum pieces' displayed ; the exhibition also gave an idea of the progress of the photoelastic method in recent years. The exhibits of recent origin revealed the amazing degree of confidence which is now placed both in model-making and in subsequent stress exploration. In fact, the method has been applied (both at University College and elsewhere) to structures of a complexity that would have surprised Prof. Coker, even in his most optimistic moments.

Recent Developments

During the Second World War, the laboratories of Profs. Coker and Filon disappeared, one literally (as a result of bombing), the other figuratively as a consequence of the rigours of war-time academic life. The revival of interest in photoelasticity in University College since then owes much to the support and encouragement of Prof. H. J. Collins and to the zeal of Colonel Jessop.

Both Coker and Filon appear to have believed that their exploitation of photoelasticity was more or less complete. But here, for once, they were quite wrong, and it is, perhaps, of interest to consider why this is so. The most striking advance has been made in three-dimensional work. This extension has been made possible by several factors. Of these, the development of a really suitable synthetic resin is a logical extension of Coker's step from glass to celluloid. With the appearance of modern epoxy casting resins, and in particular of 'Araldite *B*', practical materials have become available in adequate sizes; they possess good elastic behaviours, negligible creep, and sufficient optical sensitivity to be useful. With these new materials has come the stress-freezing technique—now more than twenty years old; this opens up an almost foolproof method for the analysis of solid models. By subjecting a model to a heating and loading cycle, it can be persuaded to 'remember' its loading system, and to retain an optical pattern which is equivalent to an elastic system of stress. The solid model can then be sectioned without disturbance of the optical effect, and a three-dimensional analysis can be made. The possibility of doing this was noted in Germany in 1935, but was apparently not known to Filon or to Coker (who was, by then, a sick man). A similar effect had been noted in glass at University College by Dr. F. C. Harris, although its implications for three-dimensional work were not recognized.

It is interesting to note that, with this development, one returns to the original difficulties of measurement which faced Coker. However, his primitive methods have been superseded by the techniques due to Tardy or Sénarmont. Sufficiently accurate measurements can now be made with strains in the model which are not more than ten times the strain in the prototype.

The interpretation of the results found from a model in terms of the corresponding full-scale structure in a different elastic material, and the effect of a tenfold increase in magnitude of strain in the model, was discussed in a review of the present state of knowledge. This was given at University College in two lectures on modern aspects of photoelasticity by Mr. C. Snell. He argued that although the position is not entirely clear, there are good theoretical and experimental reasons for transferring the stress pattern without significant change from model to prototype.

The problem of thermal stressing was exemplified in the exhibition, and the experimental difficulties that have yet to be overcome were mentioned. Dynamic stressing was also illustrated, with a demonstration that problems of dynamic elasticity can sometimes be studied by photoelastic means. In particular, periodic excitation can be investigated in this way unless the periodic time is too short for stroboscopic techniques to be adequate.

The use of optically sensitive layers to show the strain patterns in metals beyond the elastic range is probably the most recent development in photoelasticity. This technique was illustrated in two exhibits and is undoubtedly a promising new departure. Perhaps not so promising—but by no means without interest—was some apparatus (of recent origin) for investigating the optical behaviour of a moving fluid.

Photoelasticity in Engineering

These, and many other, exhibits leave no doubt about the future of photoelasticity. It has been put to use time and time again, particularly in the aircraft industry, where the economical use of material is vitally important. Now it seems clear that the methods will be widely employed in design work on nuclear engineering projects.

Historically, our knowledge of the stress–optical effect is of Scottish origin, the earliest investigations having been made by Brewster and, later, Maxwell. But practical stress exploration undoubtedly grew up in University College, London. It is most unlikely that any other institution could arrange, from its own resources, an exhibition covering so wide a range of productive work within photoelasticity—even if the earlier exhibits of purely historical interest are disregarded. This is a direct outcome of the collaboration of Profs. Coker and Filon—an engineer and a mathematician—and of the subsequent efforts of a small group of workers under the leadership of Colonel Jessop and, since his retirement, Mr. Snell.

R. E. D. BISHOP

OBITUARIES

Dr. Paul Chabanaud

DR. PAUL CHABANAUD, Chevalier de la Légion d'Honneur, well known for his researches on fishes, died on February 27 at the age of eighty-two.

Although he had been from childhood a keen amateur naturalist, Chabanaud began by preparing himself for a career in the law, but he considered this to have been a false start. Soon after the beginning of the First World War he was declared medically unfit for the Armed Forces and became a voluntary assistant to Prof. Roule at the Museum of Natural History in Paris, classifying and preparing exhibits from the collections of reptiles and amphibians.

In September 1919, Chabanaud received the blessing of the professors of the Museum to fulfil his great ambition of a collecting trip to tropical West Africa. Apart from free passage to French Guinea and free rail travel within the territory, the only financial assistance he received was a grant of ten or twelve hundred francs. He spent about eight months in the field, covering about 1,200 km. on foot, and brought back valuable collections of arthropods, reptiles, amphibians and fishes, as well as considerable ethnological material.

It was only on his return from this voyage that Chabanaud sought any remuneration for his scientific work, and in 1920 he was appointed Préparateur à l'École des Hautes Études, working in the Laboratoires des Pêches et Productions Coloniales d'Origine Animale. From this time his main studies were in ichthyology, and it was in this field that in 1936 he obtained his doctorate, with a thesis on the morphology and phylogeny of the flatfishes (Heterosomata). This penetrating study confirmed the groupings recognized by Tate Regan in 1910 and 1929, and demonstrated a better understanding of the details of flatfish structure than had been possessed by any of his predecessors. His interpretation of this classification, however, was unique. He agreed with Tate Regan that *Psettodes* was a little-modified percoid fish, diverging less from the symmetrical form than any other flatfish. But whereas Tate

Regan looked upon this genus as a survival from the base of the flatfish stem, to Chabanaud it was the latest departure from the path of percoid symmetry, and the more specialized soles and flounders were the modern twigs of earlier asymmetrical branches of the pre-percoid trunk. The fossils so far do not help to resolve this difference, for as Chabanaud himself was to describe, the main groups were already differentiated in the Upper Eocene.

The majority of Chabanaud's numerous publications after 1936 were on details of the morphology and classification of these asymmetrical fishes, in which he found an endless fascination. He applied to them a terminology of his own, which, in spite of its logical classicism, is unlikely to supersede current usage, which has 'just growed'. It was his ambition to write the second volume of the monograph of the flatfishes begun by J. R. Norman, but he began too late in life to analyse the many samples of soles and tongue-soles available to him and never arrived at a satisfactory synthesis.

Up to the eve of his last illness, Chabanaud would leave his flat in the Rue des Écoles at 8 a.m. and walk, painfully of late, to the laboratory in the Rue Cuvier to count more fin-rays and scales and cover more sheets with his endless tables. How I wish that in some Elysium it might be given him to draw from them the crystal truths that he was sure they would eventually yield ! He could be a charming host, and one of his most engaging accomplishments was the relating of reminiscences, plunging into parenthesis after parenthesis without faltering in the elegant use of his mother-tongue and never failing to emerge triumphantly in the end as from a series of Chinese puzzle-boxes.

He was quite unworldly, a man of child-like integrity and innocence of mind. He is survived by his second wife, with whom he spent many years of mutual devotion.

E. TREWAVAS

Prof. J. T. MacGregor-Morris

PROF. J. T. MACGREGOR-MORRIS died on March 18, at the age of eighty-seven. He established the Electrical Engineering Department at East London College (now Queen Mary College) in 1898, and he became the first professor of electrical engineering in this College, a position which he held until he retired in 1938.

He received his education in electrical engineering at University College, London, and, for a time, was personal assistant to Sir Ambrose Fleming. He was keenly interested in research and during the Second World War he did notable work in developing a hydrophone for submarine detection.

An important contribution to electrical engineering education by Prof. MacGregor-Morris was the manner in which during the lean years immediately following the First World War he kept research work alive in his department, despite meagre equipment and small research funds. He kept the department open on three evenings a week, and he inspired and directed the research work of students who attended on these evenings. The students were of good calibre and they did good work. Several of them have risen to important positions in the electrical industry.

Under the leadership of its professor, the Department grew steadily in prestige, and its housing and equipment improved as the years passed. A notable development was the opening of its well-known High Voltage Laboratory in 1938 with the aid of a grant from the London County Council. This Laboratory was an example of Prof. MacGregor-Morris's foresight —he was a good judge of new developments which were likely to become of major importance in electrical engineering. Another example of this was his interest in the cathode-ray tube from its earliest days. He was joint author of one of the earliest text-books dealing with these tubes.

His lectures were interesting, stimulating and unorthodox with his over-riding interest in research always intruding.

His students and particularly his research students were important personages to him. Many of them will recall with pleasure the annual 'get-together' of staff and research students at his home in Hampstead. Mrs. MacGregor-Morris always took an active part on these occasions.

He was a very active man. On most Wednesday afternoons during term time he would play a strenuous game of tennis or badminton. He was keenly interested in music and, when quite elderly, he learned to play the 'cello and became a proficient performer on this instrument. He was a devout Christian and took an active interest in missionary work.

W. J. JOHN

Dr. John Henderson, C.B.E.

DR. JOHN HENDERSON, for seventeen years director of the New Zealand Geological Survey (N.Z. Department of Scientific and Industrial Research), died suddenly at his home on March 6. Born in Dunedin in 1880, his later education was carried out at Otago Boys' High School, then at the University of Otago and Otago School of Mines. Here he completed, in 1902, his M.A. associateship of the School and B.E. (Mining).

For the next eight years he was director of Reefton School of Mines, during which time he devoted much energy to the investigation of the geological structure of the coal and gold mines of Westland and West Nelson, his thesis on the subject gaining him his D.Sc. in 1907.

In 1911 he was appointed mining geologist to the New Zealand Geological Survey. As well as keeping in touch with mining activities in the succeeding years, and reporting on numerous mines, quarries, and mineral properties of different kinds, he also reported on the geological implications of many engineering projects, for example the Arapuni Hydro-electric Dam on the Waikato River. In addition, he carried out extensive regional surveys of the geology and mineral resources of several districts. His bulletins on Reefton, Te Aroha (with J. A. Bartrum), Gisborne and Whatatutu (with M. Ongley), Mokau (with M. Ongley) and Huntly-Kawhia (with L. I. Grange) stand as lasting contributions to the geology of the Dominion.

At the request of the Fiji Government in 1923, Dr. Henderson visited and reported on the geology and mining prospects of gold-bearing quartz lodes in Vanua Levu.

Dr. Henderson, in 1928, succeeded the late P. G. Morgan as director of New Zealand Geological Survey and almost immediately encountered all the administrative difficulties and frustrations resulting from the financial stringency of the great economic depression. Nevertheless, by unremitting work he was able to keep his staff of geologists intact, and so actively to maintain the geological effort of New Zealand. Bulletins could no longer be printed, but the condensed reports, and the black-and-white geological maps of the annual reports of those years, have since proved their worth.

With the coming of better times and the greatly increased activities of Works, Railways and other Government Departments and public bodies, the requests for geological advice increased enormously. The consequent expansion of the Geological Survey was carried out over a wide field, including soil surveys and geophysical surveys. Each of these has now become a separate division of the Department of Scientific and Industrial Research. About this time Dr. Henderson represented the Dominion at the International Geological Congress in South Africa, when he was able to visit the great gold mines of Johannesburg and the Rand.

In addition to his official duties, Dr. Henderson wrote a number of papers on general geology and stratigraphy, published in the *Transactions of the Royal Society of New Zealand* and in the *N.Z. Journal of Science and Technology*. During his directorship he carried on the high tradition, so well implanted in Geological Survey routine by P. G. Morgan, of most careful and accurate editing of publications, especially of the bulletins. After retirement he acted as honorary editor (1946–49) of the *Transactions of the Royal Society of New Zealand*.

Dr. Henderson was of a modest and retiring disposition, avoiding publicity, but with a deep sense of public responsibility. His interests, and also his reading, covered a wide field. This gave him a vast amount of documented information always willingly and helpfully at the service of his colleagues. To the young geologist his wealth of knowledge and kindly interest provided a real source of inspiration.

Dr. Henderson was awarded, in 1929, the fellowship of the Royal Society of New Zealand, in 1935 the Jubilee Medal, in 1945 the Hector Medal and Award of the Royal Society of New Zealand, and in 1948 he was appointed C.B.E. J. Marwick

NEWS and VIEWS

New Foreign Members of the Royal Society : Prof. Melvin Calvin

Prof. Melvin Calvin, of the University of California, Berkeley, California, whose election to the foreign membership of the Royal Society was recently announced (see *Nature*, **183**, 1230 ; 1959), started his professional career as a control chemist in industry after the completion of his doctorate at the University of Minnesota, to which he later returned as a teaching Fellow. He then spent two years at the University of Manchester, returning in 1937 to the University of California, where he has remained ever since. His early interests were in theoretical organic chemistry and the mechanism of organic reactions.

After the Second World War Calvin took over the work initiated by Ruben on the study of photosynthesis, but employing the newly available radioisotope, carbon-14. The early results were questioned by many biologists, who from their physiological studies held strong convictions about the probable mechanism of photosynthesis ; but with the timely advent of paper chromatographic methods Calvin used these to exploit the powerful potentialities of tracer techniques. From then on progress was rapid and Calvin was gradually led to formulate a mechanism of carbon reduction in photosynthesis which is now universally accepted. From studies of photosynthesis he was led to postulate enzymic systems not then isolated but afterwards discovered both in animal and in plant tissues. The photosynthetic cycle of Calvin and his collaborators may be elaborated in the future but is unlikely to be changed in its essential features. He was awarded the Stephen Hales award of the American Society of Plant Physiologists in 1956.

The Editors regret that, due to difficulties in the printing industry, some sections of this issue of "Nature" have had to be curtailed

Calvin is the co-author of an excellent text-book on theoretical organic chemistry and his lectures have stimulated both undergraduates and research workers. He has published books on the use of isotopes and on the chemistry of metal chelate compounds. His wide interests include photochemistry and general physical chemistry as well as theoretical organic chemistry.

Prof. G. Domagk

Prof. Gerhard Domagk, recently elected a foreign member of the Royal Society, has devoted his life to the fight against some of the main scourges on mankind, against cancer and against bacterial infections including tuberculosis. A graduate of the University of Kiel, Domagk began his university career in Greifswald and Münster ; in 1927 he became head of the Research Institute for Experimental Pathology and Bacteriology of I. G. Farbenindustrie, Elberfeld, and it is there that he has carried out his successful researches for more than thirty years. Throughout this period he has, however, kept his ties with the University of Münster, where he was made personal professor in 1932.

His discovery in 1932 that an azo dye, 'prontosil', cured streptococcal infections in mice revolutionized medical thought, which had for many years proclaimed that chemotherapy of bacterial, in contrast to chemotherapy of protozoan, diseases was a utopian aim. It is well known how this discovery led to the development of the treatment of many serious infections with a variety of 'sulphonamides' ; the award of the Nobel Prize in 1939 was in recognition of this very great advance.

It is a tribute to the impetus given to chemotherapy by Domagk's discovery that when he turned to the problem of the chemotherapy of tuberculosis, there were many groups all over the world trying to tackle the same problem. So it happened that Domagk's most successful anti-tuberculous drug, isoniazid, discovered by him in 1951, was introduced into therapy independently by a group of American workers. Domagk was also the first to direct attention to the important antiseptic properties of the so-called 'inverted soaps'.

Domagk, whose interest in cancer dates back to 1928, is now mainly interested in the possibilities of chemotherapy of cancer. As a result of his recent work on animals, some compounds of promise are at present undergoing clinical trial. For the sake of mankind it is to be hoped that the success he has had in his other fields of endeavour will not fail him in this quest.

Prof. J. H. Oort

FEW astronomers have made such important contributions to the study of the structure and dynamics of the galactic system as Prof. J. H. Oort, who was recently elected to foreign membership of the Royal Society. He was among the first to recognize the importance of the high-velocity stars, interpreting the zone of avoidance of their motions in terms of the velocity of escape from the galactic system. These studies enabled him to develop Lindblad's theory of galactic rotation into the form in which it is used to-day. He developed formulæ for the effect of galactic rotation on the radial velocities and proper motions of the stars, and analysed the observational material to obtain estimates of the angular velocity and mass of the Galaxy. Another major investigation was concerned with the motions of the stars perpendicular to the galactic plane. Oort obtained a relation between the velocities of the stars and the gravitational acceleration of the Galaxy, and with the aid of models of the Galaxy he determined the density of matter in the solar neighbourhood. Since the Second World War, Oort's most important work has been his inspiration and leadership of the team of Dutch astronomers who have been investigating galactic structure with the aid of 21-cm. hydrogen radiation. It is no exaggeration to say that, under Oort's direction, the Leyden Observatory has become one of the world's leading astronomical institutions, the work of which has had, and continues to have, a profound influence on the progress of astronomy.

Prof. A. H. T. Theorell

PROF. HUGO THEORELL was also recently elected a foreign member of the Royal Society. Theorell's main work at the Nobel Medical Institute, Stockholm, has been concerned with the oxidizing enzymes, especially flavoproteins, hæmoproteins and dehydrogenases, in all of which fields he has made important contributions to knowledge during a period of more than twenty-five years. He first purified the yeast flavoprotein which had been discovered by Warburg and Christian, and later he isolated it in crystalline form. He investigated particularly the nature of the union between the flavin prosthetic group and the protein part, and showed the importance of the phosphate group in this. He also was the first to crystallize several hæmoproteins, including myoglobin and the peroxidases of milk and horseradish, and studied them in detail by physical methods, developing especially the use of measurements of magnetic susceptibility for the examination of the state of the iron atom in hæmoproteins. Theorell also investigated in great detail the structure of highly purified cytochrome *c*, established that the connexion of the porphyrin with the protein was through sulphur groups, and was ultimately able to construct a model of the structure of the part of the molecule adjoining the prosthetic group. He also carried out an important detailed study of the kinetics of the alcohol dehydrogenase system, using elegant methods depending on measurements of ultra-violet absorption and fluorescence. This led to interpretations of the apparent Michaelis constants of the various reactants in terms of the rate constants of the separate steps of the catalytic process and threw a good deal of light on the mechanism of the catalytic action of the enzyme.

Institution of Mining and Metallurgy: Awards

THE Institution of Mining and Metallurgy has announced the following awards: The Gold Medal of the Institution for 1958 to Dr. A. J. Orenstein, for long and distinguished service in the cause of the health and welfare of the workers in the mining industry, with particular reference to the Witwatersrand; honorary membership of the Institution has been conferred on Mr. W. A. C. Newman, in recognition of his services both to the Institution (of which he is a past-president) and to metallurgical education; on Brig. R. S. G. Stokes, past-president, in recognition of his services to the mining industry particularly in South Africa; and on Sir Alexander Fleck, in recognition of his outstanding services to the metallurgical industry; 'The Consolidated Gold Fields of South Africa, Limited' Gold Medal for the session 1957–58, to Mr. F. A. Williams, for his paper entitled "Performance Analyses of Screens, Hydrocyclones, Jigs and Tables used in recovering Heavy Accessory Minerals from an intensely decomposed Granite on the Jos Plateau, Nigeria" (*Trans. Inst. Min. Metall.*, **67**); and 'The Consolidated Gold Fields of South Africa, Limited' Premium of forty guineas for 1957–58, jointly to Mr. H. H. Fraser and Mr. O. E. A. Somerset, for their paper entitled "Scientific Management Principles applied to West African Mining" (*Trans. Inst. Min. Metall.*, **67**); The 'William Frecheville' Student's Prize to Mr. I. R. M. Chaston, for his paper entitled "A Simple Formula for Calculating the Approximate Capacity of a Hydrocyclone" (*Trans. Inst. Min. Metall.*, **67**).

Leverhulme Research Awards, 1959

THE Trustees have approved, among others, the following research fellowships and grants tenable for periods up to two years. *Fellowship:* Dr. K. R. S. Morris (epidemiologist attached to the American Foundation for Tropical Medicine, Inc., Harbel, Liberia) for a historical and epidemiological study of the movement of sleeping sickness across Africa. *Research grants:* Maurice Black (fellow and director of studies, Trinity College, University of Cambridge) to complete a study of limestone deposition in the Bahama Islands; Geoffrey Bownas (lecturer in Chinese and Japanese studies, University of Oxford) for a comparative study of urban and rural life in Shiga Prefecture, Japan; Dr. N. H. Hartshorne (reader in chemical microscopy, University of Leeds) for a critical study of the applications of polarization microscopy in chemical and biological research and practice; Dr. K. J. Ivin (lecturer in physical chemistry, University of Leeds) to study the solution properties of polymers; G. G. Lemon (lecturer in petrology and economic geology, University College of Wales, Cardiff) to study the metamorphic rocks of the County Sligo area, Eire; Mrs. Lily Newton (lately professor of botany, University College of Wales, Aberystwyth) to study marine algae, especially those with walls yielding carrageenin and algin; D. T. Whiteside (St. Catharine's College, University of Cambridge) for an examination of the mathematical section of the Portsmouth Collection of Newton manuscripts.

A Lunar Radio Communication Link across the Atlantic

IN a series of experiments carried out between May 11 and May 14 a lunar radio communication link was successfully established between the Jodrell Bank Experimental Station in Cheshire and the Air Force Cambridge Research Center at Bedford, Massachusetts. A 1-kW. frequency-modulated transmitter working on 201·00 Mc./s. was used with the 250-ft. steerable radio telescope at Jodrell Bank. In the United States an 84-ft. radio telescope was used with receivers of various bandwidths from ± 2·5 to ± 10 kc./s. Similar receivers were also used on the telescope at Jodrell Bank for monitoring the local lunar returns. The aerial systems were circularly polarized in order to avoid the deep fading caused by Faraday rotation in the ionosphere. A series of experiments lasting for about 40 hr. included the study of the transmission of audio tones up to 15 kc./s., the transmission of messages by slow Morse, and tests of the intelligibility of speech and quality of music. The tones and Morse were received in the United States without difficulty. Speech as received back at Jodrell Bank was nearly always clear and intelligible, but only occasionally so in America because of the low signal-to-noise ratio of their equipment.

Although trans-Atlantic reception of the lunar radar pulses transmitted from Jodrell Bank was reported in 1958, the recent experiments are believed to be the first to demonstrate the feasibility of a true lunar communication link. The commercial interest in long-distance transmission secure from ionospheric and terrestrial interference will undoubtedly stimulate further developments in this field. Transmitters of somewhat greater power working in the microwave band, where the potentialities of low-noise maser or parametric receivers can be realized, should enable the size of the radio telescopes to be reduced, and at the same time provide sufficient signal-strength to ensure speech intelligibility under all conditions. This work was carried out as part of a joint programme between Jodrell Bank and the Air Force Cambridge Research Center, but the early realization of the successful lunar link was made possible by the interest of Pye Telecommunications, Ltd., which provided the transmitter and receivers.

Creation of the College of Technologists

THE establishment of the College of Technologists was announced on May 20 by the Governing Body of the National Council for Technological Awards, the chairman of which is Lord Hives. The College will administer the award of Membership of the College of Technologists (M.C.T.) which the National Council proposes to create as a qualification higher than the Diploma in Technology. The College of Technologists will operate within the framework of the National Council for Technological Awards and will be served by the same administrative staff. A Board of Scientific and Industrial Studies is to be responsible for the academic and industrial aspects of the administration of the award. The governing body of the National Council has met as the Court of the College and the following appointments to the Board were made: Sir Arnold Hall, managing director, Bristol Siddeley Engines, Ltd. (*chairman*); Mr. A. W. J. Chisholm (head of the Department of Mechanical Engineering, Royal Technical College, Salford); Dr. H. O. J. Collier (director of pharmacological research, Parke Davis and Co., Ltd.); Dr. J. W. Cook (vice-chancellor, University of Exeter); Prof. P. V. Danckwerts (professor of chemical engineering science, Imperial College of Science and Technology, London, and Shell professor-elect of chemical engineering, Cambridge); Prof. E. Giffen (professor of civil and mechanical engineering, Queen Mary College, London); Dr. A. A. Griffith (research consultant, Rolls-Royce, Ltd.); Sir Stanley Harley (managing director, Coventry Gauge and Tool Co., Ltd.); Prof. A. J. Murphy (principal, Cranfield College of Aeronautics); Mr. P. E. Sleight (head of the Civil Engineering and Building Department, Brighton Technical College); Dr. G. B. B. M. Sutherland (director, National Physical Laboratory); Dr. J. S. Tait (principal, Northampton College of Advanced Technology, London); Dr. J. Topping (principal, Brunel College of Technology); Dr. R. C. G. Williams (chief engineer, Philips Electrical, Ltd.).

In addition to the members listed, the Court intends to appoint to the Board one more member of the teaching staff of a College of Advanced Technology. A further statement will be issued as soon as possible giving the details which will be needed for the submission of applications for registration as candidates for membership of the College of Technologists.

Jobs for School Leavers

INTERESTING proposals for dealing with the 'bulge' have been put forward by John Wellens, an industrial training consultant. This year some 900,000 boys and girls will reach the age of fifteen and in 1962 the figure will rise to 1,000,000. As at present organized, industry and commerce are quite unprepared to absorb the considerable extra number of school-leavers who owe their existence to increased birth-rate during and immediately after the War. The training facilities available for those that can be absorbed are inadequate by the most elementary of standards. To deal with the situation, Wellens suggests that a national industrial training agency should be formed, responsible to the Minister of Labour and National Service, and that the existing Industrial Training Council should act as an advisory body to the Agency ("The Bulge: Its Industrial Impact. A National Plan". John Wellens Organization, 24 Morsley Road, Grasscroft, nr. Oldham. 5*s*.). Details of the way in which the agency would work are elaborated as well as the main lines it should follow. It is doubtful whether the somewhat impractical proposals will command any wide support.

Government Support for Research in Water Supply

THE Department of Scientific and Industrial Research is to give financial support to the Water Research Association. The council of the Association has been strengthened by the appointment of Mr. J. E. Beddoe, assistant secretary, Water Division, Ministry of Housing and Local Government, of Dr. B. A. Southgate, director, Water Pollution Research Laboratory, and of Mr. G. A. McMillan, Department of Scientific and Industrial Research. The Department of Scientific and Industrial Research has appointed Prof. F. H. Garner (Birmingham) and Mr. C. S. Tanner (Imperial Chemical Industries, Ltd.) as 'visitors'.

The Water Research Association commenced with an income of £11,000. This rose to more than £20,000, but the research needs of the water industry are, with the increasing demands for water, so pressing that the water undertakings have decided to double their subscription to the Research Association and the Department of Scientific and Industrial Research has offered grant-in-aid up to £27,000. With an anticipated income of £72,000 the Association is moving its laboratories from Surrey to a site on the Thames in Buckinghamshire, where with an increased staff it can augment its present programme of work on the coagulation process of water purification, leak detection and plastic pipes, by the addition of filtration studies, dewatering of sludge, biological and chemical analytical methods and algal growth control. It will also pursue some of the hydrological interests of the water industry.

Science Information News

The National Science Foundation is issuing a new bi-monthly bulletin, *Science Information News* (1, No. 1; February–March 1959. Published bimonthly. Annual subscription, 1.75 dollars. Single copies, 25 cents. Washington, D.C.: National Science Foundation, 1959. Obtainable from the Superintendent of Documents, U.S. Government Printing Office), to provide a medium for reporting new and improved methods of disseminating scientific information and news of activities in this field. The first issue (February–March 1959) deals with the establishment by the National Science Foundation of its Science Information Service, the appointment of the Science Information Council and the establishment of the Federal Advisory Committee on Scientific Information and of a Research Advisory Service on Information Processing. There are, however, notes on the International Conference on Information Processing to be held in Paris during June 13–23, on the expanded programme planned by the Office of Critical Tables of the National Academy of Sciences–National Research Council, the study by the Columbia University Bureau of Applied Social Research of the flow of scientific information among scientists, and the study by the Case Institute of Technology of scientific communication among chemists. It is hoped that in future issues the bulk of the bulletin will comprise material contributed by readers and outside the Foundation's own activities in this field.

Royal College of Science and Technology of Glasgow

The latest annual report of the Royal College of Science and Technology, Glasgow, records no major building developments in 1957–58, but of a number of alterations the largest was the conversion of St. Paul's Church for the use of the School of Navigation. This building has yielded accommodation of a high standard and the rooms previously occupied by the school have been taken over by the Department of Natural Philosophy. Full-time students increased from 1,508 in 1956–57 to 1,662, part-time day students from 1,119 to 1,349, while evening students decreased from 2,346 to 2,109. Besides a list of titles of theses presented by 21 members awarded higher degrees by the University of Glasgow, and of those approved for the awards of the postgraduate diploma of the College, the report includes a list of recent publications by members of the College. Further information on research work in progress is given in the Research Report for the Session 1957–58, in which abstracts of most of the publications listed are appended to the summaries of the work in progress in the various Departments.

Jubilee of Queen's University, Belfast

It is just fifty years since, under the Irish Universities Act of 1908, The Queen's College, Belfast, founded in 1845 as part of a government plan for the extension of university education in Ireland, was dissolved and The Queen's University of Belfast was established. The retention of the title 'Queen's' for the new university was intended to show continuity with the foundation of 1845 and to proclaim adherence to the principle of non-sectarian education on which the old Queen's College (and those at Cork and Galway) had been established. This continuity is reflected in the short history of the College and the University, written by Prof. J. C. Beckett, which has been issued as a booklet (Queen's: a Short History of Queen's College, Belfast, and the Queen's University of Belfast. Pp. 10. 6*d*. Belfast: Queen's University, 1959), although the developments of the past fifty years occupy about half the account.

A new building, called the David Keir Building, to accommodate the Departments of Engineering, Chemistry, Zoology and Botany, was opened by the Duke of Edinburgh on May 21. The plans for this extension were described in *Nature* of February 19, 1955, p. 323.

Museum Treatment of Weakened Fabrics

In the issue of the *Museums Journal* of January 1959, Mr. E. R. Beecher describes a method of conserving fragile woven fabric by heat-sealing to prepared nylon net, allowing the intimate overall support provided by adhesion, while preserving the intrinsic textile quality of flexibility, of which some vestige may survive even in the worst example. The nylon net used is described technically as 15 denier 100 per cent bobbin with a count of 42/43 per sq. in. It is sold as 'Nylusion tulle'. Textile fabric thus mounted—full details are to be found in the article quoted—can be examined on both sides. The method is also reversible as a touch of acetone will dissolve the film on the nylon and allow it to be lifted away.

Resin-bonded Coatings of Polytetrafluoroethylene

Thin films of polytetrafluoroethylene on metal and other surfaces are in use because of their properties of low friction, stability at high temperatures, resistance to chemical attack and weak adhesion. Methods of fixing the film on to the base material involve sintering at 400° C., and for this reason films on rubber, plastics, wood and certain metals have not easily been obtained. A dispersion of polytetrafluoroethylene, under the trade name 'Emralon' (Acheson Colloid, Ltd.), has now become available and enables a coating of the polymer to be resin-bonded at low temperatures to a variety of surfaces. The advantage of this coating over the pure polytetrafluoroethylene film is its applicability to heat-sensitive surfaces, although, in addition, stronger adhesion and greater resistance to wear and corrosion are claimed. Of the two grades available, one uses a phenolic resin binder which can be applied by air spray and requires curing for one hour at 150° C.; the second contains a thermoplastic resin binder and needs no heat curing, so that it can be applied to surfaces where baking, even at 150° C., is impracticable.

Geological Society of London: Officers

At the recent annual general meeting of the Geological Society of London the following officers were elected: *President*, Dr. C. J. Stubblefield; *Secretaries*, Mr. J. M. Edmonds and Dr. P. A. Sabine; *Foreign Secretary*, Prof. O. T. Jones; *Treasurer*, Mr. P. Evans; *Vice-Presidents*, Mr. A. J. Butler, Prof. L. Hawkes, Mr. T. C. Nicholas, and Dr. E. I. White.

Institution of Metallurgists: Officers

The following were recently elected to office in the Institution of Metallurgists: *President*, Prof. A. J. Murphy (College of Aeronautics, Cranfield); *President-elect*, W. E. Bardgett (United Steel Companies, Ltd.); *Vice-Presidents*, Dr. W. O. Alexander (Imperial Chemical Industries, Ltd., Metals Division), Prof. J. W. Cuthbertson (University of Nottingham); *Hon. Treasurer*, Dr. E. G. West (Aluminium Development Association).

Royal Society of South Africa: Officers

The following were recently elected to office for 1959 in the Royal Society of South Africa: *President*, A. J. H. Goodwin; *Hon. General Secretary*, W. J. Talbot; *Hon. Treasurer*, Dr. N. Sapeika; *Acting Hon. Editor of Transactions*, Dr. S. Amdurer; *Hon. Librarian*, Dr. J. H. Day. *Other Members of Council*, Dr. S. H. Haughton, Dr. F. G. Holliman, Dr. W. E. Isaac, Dr. R. F. Lawrence, Dr. R. H. Marloth, Dr. S. M. Naudé, Dr. S. H. Skaife, Dr. R. H. Stoy, and Dr. C. L. Wicht.

The Night Sky in June

New moon occurs on June 6d. 11h. 53m. U.T. and full moon on June 20d. 20h. 00m. The following conjunctions with the Moon take place: June 10d. 15h., Venus 7° N.; June 10d. 18h., Mars 6° N.; June 18d. 11h., Jupiter 3° S.; June 21d. 05h., Saturn 4° S. In addition to these conjunctions with the Moon, Venus is in conjunction with Mars on June 14d. 13h., Venus being 0·8° N., and Mercury with Pollux on June 24d. 09m., Mercury being 5·0° S. Mercury will be visible for a short time after sunset during the second half of the month. Venus is an evening star, visible in the south-west after sunset. Conditions are favourable for observation. Venus sets at 23h. 25m., 23h. 05m. and 22h. 30m. on June 1, 15 and 30, respectively; its stellar magnitude is − 3·9. Its distance decreases during the month from 82 to 60 million miles and the visible portion of the apparent disk decreases from 0·607 to 0·455. Mars is in Cancer during the month. It sets at 23h. 30m., 23h. 00m. and 22h. 15m. at the beginning, middle and end of the month, respectively. Its stellar magnitude is about + 1·9; it is rapidly approaching conjunction, and is low in the west after sunset. Jupiter sets at 3h. 20m., 2h. 20m. and 1h. 10m. on June 1, 15 and 30, respectively. It is in retrograde motion in Libra. The stellar magnitude of Jupiter is − 2·0; its distance is approximately 420 million miles. Saturn is in Sagittarius, rising at 21h. 55m., 20h. 55m. and 19h. 40m. at the beginning, middle and end of the month, respectively. Its stellar magnitude is + 0·3 and its distance is approximately 850 million miles. There is one occultation of a star brighter than magnitude 6 visible at Greenwich: June 11d. 21h. 21·2m., 162 B. Vir. (*D*). *D* refers to disappearance. The summer solstice occurs on June 22d. 04h.

Announcements

Dr. Louis Essen, a senior principal scientific officer at the National Physical Laboratory, has been awarded the A. S. Popov's Gold Medal by the Academy of Sciences of the U.S.S.R. This award is for the most distinguished scientific work in the field of radio-engineering performed during the period 1956–58. Dr. Essen has also recently received the first Wolfe Award of the Department of Scientific and Industrial Research (see *Nature*, 183, 930; 1959). The work of scientists from all countries is considered, but this is the first time that it has been awarded to a scientist outside the Soviet Union.

Prof. W. M. Elsasser, professor of theoretical physics at the Scripps Institution of Oceanography and the University of California, La Jolla, California, has been awarded the William Bowie Medal. The Medal is awarded for outstanding contributions to the geophysical sciences.

Dr. Robert T. Parker has been appointed head of the Banbury and Geneva offices of the Aluminium Laboratories, Ltd., in succession to Mr. R. D. Hamer.

Dr. Herman H. Goldstine has been appointed resident manager of the Lamb Estate Research Center of the International Business Machines Corporation, Cortlandt, New York. As resident manager, he will be responsible for IBM research on business theory, psychology, programming, information theory, mathematics, pattern recognition and operational research. Dr. H. J. Greenberg has been appointed manager of the Mathematics Theory Department of the Lamb Estate Research Center.

The Fulmer Research Institute, at Stoke Poges, Bucks., will hold an open day on July 16. Attendance will be by invitation only.

The autumn meeting of the Radiofrequency Spectroscopy Group, which will be held at the Clarendon Laboratory, Oxford, during September 17–18, is to be devoted to the radio-frequency spectroscopy of free atoms and molecules, with sessions on atomic beam and optical methods, microwave gaseous spectroscopy and the measurement of fundamental constants by radio-frequency methods. Registration forms (with requests for accommodation, which must be returned before July 1) can be obtained from Prof. B. Bleaney, Clarendon Laboratory, Oxford.

An International Oceanographic Congress, sponsored by the American Association for the Advancement of Science in co-operation with Unesco and the International Council of Scientific Unions, will be held in the United Nations building, New York, during August 30–September 12. Further information can be obtained from Dr. Mary Sears, Woods Hole Oceanographic Institution, Mass.

The Ninth International Botanical Congress will be held in Montreal, during August 19–29, at the University of Montreal, McGill University and Sir George Williams College, under the auspices of the Canadian Department of Agriculture. Dr. W. P. Thompson, president of the University of Saskatchewan, has been elected president of the Congress. The programme will be conducted in sixteen sections and will deal with all aspects of botany in its broadest sense, including plant production, breeding, and protection and their implications for agriculture and forestry. Inquiries should be directed to the secretary general, Dr. C. Frankton, Ninth International Botanical Congress, Science Service Building, Ottawa, Ontario.

ANTARCTIC METEOROLOGY

A SYMPOSIUM on "Antarctic Meteorology" was held in Melbourne during February 18–25. It was attended by meteorologists from eleven countries. About half the participants had been in the Antarctic during the preceding year, and this gave the discussion an added interest and a feeling of immediacy. The preparatory work carried out at the Commonwealth Bureau of Meteorology, and the smooth organization under the chairmanship of W. J. Gibbs, as well as the friendly hospitality, contributed to the success of the meeting.

The following topics were discussed in seven successive sessions, each with its own session chairman: (1) local effects (K. Langlo); (2) synoptic analysis and forecasting (J. Van Mieghem); (3) synoptic influences on lower latitudes (J. F. Gabites); (4) circulation studies (W. J. Gibbs); (5) snow and ice characteristics (G. de Q. Robin); (6) heat and mass exchanges (C. H. B. Priestly); (7) climatological aspects (J. J. Taljaard).

In practice, certain themes went through the whole symposium and were discussed repeatedly in different sessions from different points of view. One of these was the katabatic wind, which is one of the most spectacular features of antarctic meteorology. Descriptions of local katabatic winds at Mawson, Wilkes, and over the ice cap were given by P. J. R. Shaw, J. Zimmerman and K. B. Mather. The abrupt onset of katabatic winds at D'Urville and other coastal places may be accompanied by an advancing wall of drifting snow; this so-called Loewe's phenomenon was described by B. Valtat. B. L. Dzerdzeevski discussed the effect of the local topography and of the general synoptic situation upon the genesis of the katabatic winds and G. M. Tauber showed that their intensity depends on cyclonic activity over the oceans near the coast. Tauber also discussed the annual and diurnal variation of these winds in coastal regions and suggested that the diurnal variations must cause the turbulent vertical transport of heat to have a maximum during night time. R. H. Clarke described model studies carried out with the aid of a cold dome in a rotating dish pan. One of the most interesting papers on katabatic winds was presented by F. K. Ball. It gave the theory of airflow under an inversion along a rough, inclined surface. The theory indicates that katabatic stream lines should form an angle of about 40° with the fall line. Along the coast, this causes relatively strong winds at the eastern side of a headland or on the western shores of a bay. It also causes particularly strong katabatic winds in the south-west quadrant of off-shore depressions. These theoretical predictions are in good agreement with observations and with Tauber's investigations.

Another subject which came up repeatedly in different sessions was the intense heating which occurs in the antarctic stratosphere in spring. The antarctic stratosphere at 20 km. cools gradually by about 60° C. from February to September. With the return of the Sun the stratosphere warms up again; a large part of the warming (65 per cent) is accomplished within a few weeks towards the end of October or early November. K. Hanson presented a case-study of this explosive stratospheric warming over the Antarctic in October 1958. Conditions in 1957 were described by E. Flowers. Comparing arctic and antarctic conditions, H. Wexler (whose paper was presented in his absence by M. J. Rubin) directed attention to the fact that the heating in the Arctic is slightly less pronounced and that it occurs before the return of the Sun in February. In the Antarctic it occurs well after the return of the Sun. Wexler explained the spectacular warming of the polar stratosphere by a change in the circulation patterns which leads to large-scale subsidence. This view is not easily reconciled with investigations into advection across the antarctic boundary by M. J. Rubin, whose studies showed no evidence of systematic divergence from the Antarctic in the troposphere and lower stratosphere during summer. Rubin, however, did not study specifically the period in which the stratospheric heating occurs. E. B. Kraus showed that the heating cannot be due to direct absorption of solar radiation. He suggested that it may be caused by advection of moist warm air in the troposphere which results in a change in the long wave-lengths radiation balance above. This view would be in agreement with Hanson's case-study, which indicates a warming of the lower polar troposphere a few days before the rapid stratosphere heating occurred.

As regards equipment, much interest centred on automatic weather recording systems. American automatically reporting weather stations which did not require manual erection and could be dropped from the air were described by W. S. Lanterman. An automatic non-recording climatological station which had been left by the Japanese expedition at Syowa Bay during winter 1958 was discussed by Y. Morita and N. Murakoshi. Traps to measure the lateral transport of snow by drifting were tested by M. Mellor at Mawson. From an analysis of these drift measurements it was deduced by Mellor and U. Radok that the lateral transport of snow was even larger than had been anticipated hitherto. To gain maximum height for upper air measurements a special balloon valve had been developed at the University of Melbourne. V. D. Hopper stated that balloons equipped with this valve reached generally a height of 35 km. with a maximum of 43·5 km. The result of ozone observations at Halley Bay were described by J. MacDowall.

J. F. Gabites gave a lucid account of the antarctic heat balance. He found the flow of heat across 55° S. to be of the same order or only a little higher than the flow across 55° N. in spite of the greater meridional temperature difference. This could be explained by the smaller effect of friction over the ocean-covered southern hemisphere, which allows the establishment of greater vertical wind gradients and therefore greater horizontal temperature and density gradients.

Circulation in the upper air was the subject of a paper by W. B. Moreland and was also discussed in several other contributions. A stratospheric jet is a well-marked feature of the winter circulation. As in the Arctic, this polar night jet appears to be synoptically separated from the systems of the troposphere. There are, however, significant differences between the two polar regions. In the Arctic the jet core is commonly found at the 25-mb. level; in the south it occurs at a lower elevation. The jet stream persists there also later into the polar day, as may be expected from the later heating of the antarctic stratosphere. It has not been possible so far to investigate synoptically the effect of the final collapse in spring of the polar night jet upon the circulation pattern in lower latitudes.

The scarcity of observations from the Southern Ocean area inevitably affected general circulation studies and the discussion of the interaction between the Antarctic and lower latitudes. In presenting his paper on antarctic synoptic analyses, W. J. Gibbs suggested that the presence and the main features of cyclones and anticyclones can be diagnosed by the analyst though there was still considerable doubt about the reality of frontal analyses. Synoptic studies of cold outbreaks and surges had been prepared by a number of Australian authors (A. K. Hannay, R. Falconer and H. M. Treloar, F. A. Berson and U. Radok). Circulation studies based on synoptic material were presented by J. Langford, I. S. Kerr, H. van Loon and S. Karelski.

Synoptic conditions over the antarctic ice cap itself are now reasonably well known for the first time. The communication system required to achieve this end was described by T. I. Gray, jun. It appears that cyclones do occasionally penetrate deep into the Antarctic and that fronts move sometimes right across the South Pole, though this occurs not as often as is probably the case in the north. In general, high-latitude cyclones seem to move sluggishly along the coast.

The happy international co-operation established between meteorologists in the Antarctic is perhaps symbolized by a paper submitted by P. D. Astapenko (U.S.S.R.) which was based on a joint investigation by him, J. Alt (France) and M. Ropar (United States). It is hoped that this co-operation will be continued in the International Antarctic Analysis Centre which is now being set up under the ægis of the Australian Bureau of Meteorology at Melbourne and that the work carried out there will lead to a better understanding of meteorological problems as a whole.

E. B. Kraus

HYDROGEN LIQUEFACTION

The use of liquid hydrogen, first produced and collected by Dewar at the Royal Institution in 1898, has, until recently, been largely confined to the laboratory. With a normal boiling point of 20·4° K. it provides a convenient means of controlling the temperature for experiments in the range 14°–90° K. and it is used as a precooling agent in the liquefaction of helium.

On March 12, a one-day symposium on "Hydrogen Liquefaction and Associated Techniques", organized by the Low Temperature Group of the Physical Society, was held at the Institute of Physics in London, and it was evident from the attendance at the meeting, as well as the topics discussed, that interest in the liquefaction of hydrogen on an industrial scale is developing in Great Britain.

The morning session, under the chairmanship of Dr. P. H. Sykes, was opened by Prof. G. O. Jones (Queen Mary College, London), who spoke of the applications of liquid hydrogen in pure research. He pointed out that it is necessary to go well below temperatures obtainable with liquid hydrogen in order to study the interesting features of many phenomena. Nevertheless, liquid hydrogen is of great technical assistance in many experiments. In optical spectroscopy, for example, the reduction in thermal motion of atoms at low temperatures results in a decreased Doppler broadening of spectral lines. The use of liquid hydrogen in bubble chambers, where it may form both a target and a detector for nuclear reactions, has also proved of great value.

In certain experiments, however, there is little point in working at temperatures below 20° K. For example, the thermal expansion coefficients of most substances and variations in such properties of the solidified inert gases as the density, compressibility and refractive index become so small below 20° K. that they are difficult to measure with precision. Such experiments may very conveniently be performed in miniature hydrogen liquefiers with about 100 ml. of liquid and in which liquefaction commences some 15 min. after starting at room temperature.

The design and construction of small-scale liquefiers were discussed by Dr. D. H. Parkinson (Radar Research Establishment, Malvern), who emphasized the ease with which liquid hydrogen may be produced in the laboratory with relatively simple and inexpensive apparatus. High-pressure hydrogen, usually from a cylinder, is precooled with liquid nitrogen and then expanded at a valve into a reservoir. A proportion of the gas liquefies and the remainder is used to cool the incoming high-pressure gas by means of a heat exchanger between the liquid hydrogen and nitrogen stages. The yield of liquid depends rather critically on the pressure and precooling temperature; for example, a standard 120 cu. ft. capacity cylinder exhausted from 120 to 50 atmospheres would yield 0·36 litre of liquid if the gas were precooled to 77° K. and 0·55 litre with a precooling temperature of 65° K. Impurities, usually amounting to about 0·1 per cent in commercial hydrogen, must be removed from the gas or they will solidify and block the liquefier tubes, and 150 gm. of activated charcoal cooled in liquid nitrogen was recommended as an adequate absorber for each cylinder of gas.

The use of liquid hydrogen as a source of 'cold' has already been mentioned, and an application to the production of a beam of low-energy neutrons was described by Dr. F. J. Webb (Atomic Energy Research Establishment, Harwell). Neutrons from a reactor with, say, a heavy-water moderator at a temperature of 50° C. are thermal neutrons, that is, slow neutrons with energies of the same order as the thermal energies of atoms in a solid. They are spread over a range of values with the greatest number possessing energies corresponding to a de Broglie wave-length of about 1 A. In certain diffraction experiments, however, it is necessary to employ neutrons with wave-lengths greater than 4 A., the number of which is relatively small compared with those of 1 A. wave-length. Since the thermal energy is proportional to the absolute temperature, the kinetic energies of the neutrons may be reduced, and their wave-lengths correspondingly increased, by using liquid hydrogen as a moderator. In the *Dido* reactor at Harwell, a small hydrogen liquefier feeds a 3-in. diameter container placed in the neutron beam and the liquid hydrogen moderator results in a gain of the order of

25 in the flux of neutrons of the required wavelength.

Another application of liquid hydrogen to pure research was described by Mr. C. van Zyl (University College, London), who spoke of its use as a scattering target for high-energy particles. Interactions between two particles such as the proton and the neutron are being investigated as an approach to an understanding of the many-body problem. By employing three targets, one of liquid hydrogen, one of liquid deuterium, and a blank target to eliminate background scattering, it is possible to study *n–p*, *p–n*, *n–n* and *p–p* reactions in the same apparatus.

One of the difficulties encountered in building apparatus for low-temperature work is that of providing vacuum-tight windows for particles or radiation without causing appreciable absorption or scattering. Mr. van Zyl described windows for the target chambers made of thin (0·002 in.) 'Terylene' film which will contain liquid hydrogen when the chambers are surrounded by a high vacuum.

As every schoolboy knows, the considerable size of a space rocket is largely accounted for by the quantity of fuel required to deliver a given load, and the search for more exotic fuels proceeds apace. The ultimate performance of a ballistic vehicle depends upon its 'burn-out' velocity, and this is inversely proportional to the square root of the molecular weight of the fuel. Thus, the best rocket fuels have low molecular weights and are generally rich in hydrogen. From this aspect, liquid hydrogen is obviously a desirable choice, and in the afternoon session, under the chairmanship of Dr. M. Ruhemann, the possibilities were discussed by Mr. A. V. Cleaver (Rolls Royce, Ltd.).

It is estimated that combustion of hydrogen–oxygen mixtures would increase the thrust by some 40 or 50 per cent over that obtainable with conventional kerosene and liquid oxygen fuels. Against this must be set the complications of accommodating a liquid of low boiling point and low density which would tend to reduce the quantity of propellant carried by the rocket. However, recent improvements in the construction of fuel tanks, so that they contribute to the structural rigidity of the rocket and reduce its unladen weight, would seem to make the use of liquid hydrogen more feasible. Although no work is being conducted in Britain, encouraging results have been achieved in the United States with small rocket motors using liquid hydrogen and liquid oxygen.

Clearly, if liquid hydrogen were successfully employed as a fuel, the demand would exceed present production capacity very considerably. With this possibility in mind, Mr. W. L. Seddon (Petrocarbon Developments, Ltd.) presented a design study of a plant capable of producing 2 tons (about 30,000 litres) of liquid hydrogen per hour. This may be compared with one of the few large plants in existence, that at Boulder, Colorado, with a potential capacity of 600 litres per hour.

Hydrogen gas would be derived from oil refinery light hydrocarbon products, and since it is difficult to predict the future demand for liquid hydrogen the economics of the scheme were based on the production of heavy water by distillation. Liquefaction would take place by Joule–Thomson expansion of compressed hydrogen, but one difficulty would be the removal of impurity, ½ per cent of nitrogen present in the feed gas resulting in the deposition of 300 lb. of solid per hour. It was therefore proposed to precool the feed gas to about 35° K. with the aid of expansion turbines and expand the gas from a pressure of about 16 atmospheres. Under these conditions, the efficiency of the Joule–Thomson process remains fairly high and a considerable proportion of impurity is carried through the expansion valve and deposited in the liquid reservoir, where it may easily be removed.

The capital cost of such a plant is in the region of £6,000,000, and the estimated price of the product, allowing for the sale of heavy water as a by-product, is £200 per ton. Liquid hydrogen produced on this scale would therefore work out at a cost of about 1*s*. a gallon, comparing surprisingly favourably with hydrocarbon fuels at, say, 4*s*. 8*d*. a gallon.

On a somewhat smaller scale, a paper by Dr. B. Shaw and Mr. W. H. Denton dealt with the problem of coping with a varying demand at the Atomic Energy Research Establishment, Harwell, by storing liquid hydrogen in 50-litre Dewar vessels. Hydrogen consists of molecules in two different rotational states, the equilibrium concentration being 75 per cent *ortho*-hydrogen and 25 per cent *para*-hydrogen, but the liquid is slowly converted to the *para* form with evolution of heat. In storage, therefore, liquid is lost by *ortho–para* conversion and it is usually more desirable to induce the conversion before liquefaction by passing the high-pressure gas over a catalyst such as ferric oxide or activated charcoal at low temperatures. Dr. Shaw presented figures showing that, for short-term storage, greater overall economy is gained by carrying out partial conversion at 80° K. than by converting completely to the para form at 20° K. The total loss from a 50-litre Dewar vessel with liquid nitrogen shielding may be as low as 0·18 litre per day.

For storage on a large scale, however, a vacuum-insulated vessel employing a liquid nitrogen radiation shield would be unduly large and complicated and the feasibility of using thermal insulation similar to that now employed in liquid nitrogen and oxygen storage vessels was discussed in a paper by Mr. K. C. Smith and Dr. J. B. Gardner (British Oxygen Research and Development). In these vessels, the liquid is surrounded by a space evacuated to a pressure of 10^{-1} mm. mercury and packed with an insulating powder. For liquid hydrogen, the loss from such a vessel would chiefly be due to radiation, and Mr. Smith described measurements of the overall thermal conductivity resulting from the addition of reflecting particles, such as aluminium powder, to the powders commonly in use. They show a significant decrease in thermal conductivity and indicate that the thickness of insulation need not be inconveniently great in, for example, a vessel of 10 ft. in diameter. Similar considerations are being applied to the design of transfer lines for large quantities of liquid.

The question of safety must be given prime consideration when dealing with liquid hydrogen, and some general remarks were made by Dr. A. J. Croft (Clarendon Laboratory, Oxford), who stressed the importance of making provision for possible human errors in operating liquefiers. Many of the precautions are common to any equipment containing low boiling-point liquids or gases at high pressure, as, for example, the fitting of relief valves to prevent the pressure rising above a safe value. One must also adopt the precautions normal when dealing with a highly inflammable liquid or explosive vapour, such as adequate ventilation of buildings. The consequences of a mishap should be minimized by partly enclosing liquefying plant by blast walls and by operating it remotely. This, of course, is not always feasible, particularly with small-scale laboratory installations.

Happily, there have been few serious accidents attributable to the use of liquid hydrogen, and reasonable and sensible safety precautions would appear to suffice. Judging by the papers and discussions presented at this symposium, it is conceivable that, in the future, liquid hydrogen will be produced and handled on a scale and with a facility comparable to that encountered to-day with liquid oxygen.

D. H. BOWEN

PARASITOLOGY

THE first meeting outside London of the Parasitology Group of the Institute of Biology was held in the Zoology Department, University of Edinburgh, during March 19–21. It was the longest session so far held and the range of topics discussed was limited only by the general heading of "Parasitology".

Twenty-five papers were read, covering subjects as varied as the use of antigen–antibody reactions to differentiate species and strains of *Entamoeba* (V. Zaman), and the morphology, function and taxonomic status of the adhesive apparatus of Amphibdellatid parasites of electric rays (J. Llewellyn).

Some of the speakers were concerned with the mechanisms which trigger the changes in parasite life-histories. E. W. McConnachie reviewed the possibility that the onset of sexual reproduction of some parasites is related to hormonal changes in the host, and outlined her preliminary experiments with *Opalina* in frogs which tentatively support this view. Assuming a direct effect of the host's hormones on the parasite, one would have to postulate the presence of such hormones at the site of parasitism, which, for *Opalina*, is the lumen of the frog's rectum. Coccidian Protozoa would seem to be in a more favourable position to be influenced by systemic changes in the host since they develop in the epithelial tissues of the gut, but S. F. M. Davies showed that no mechanism of this kind was needed by *Eimeria necatrix* in chicks, the sexual phase of development being initiated by second-generation merozoites irrespective of the physiological state of the host.

The evolution of a temperature trigger mechanism in the life-cycle of certain tapeworms was argued by C. A. Hopkins on the basis of ecological studies on *Proteocephalus filicollis* in sticklebacks. He showed that in the north of Britain very few of the immature stages of these worms complete their development, even though they become successfully established in the fish host. Comparison with the state of affairs in the south suggested that low temperature can arrest development of such a species, limited, as it is, to cold-blooded hosts. An elegant solution to the parasite's problem would be the inclusion in the life-cycle of an 'incubator' in the form of a warm-blooded host. Hopkins suggested that this may have happened in the case of three-host pseudophyllidean tapeworms, since a rise in temperature is almost sufficient on its own to mature the plerocercoids of some of these parasites.

Mechanisms which enable free-living stages to locate their hosts were considered in two papers, one by C. A. Wright, the other by C. Ellenby and A. B. Gilbert. The former put forward evidence in favour of a response by trematode miracidia to substances exuded by their molluscan hosts. Ellenby and Gilbert presented a progress report on work with the hatching factor of potato root eelworm and showed that their results were still consistent with the view that an unsaturated lactone ring is diagnostic of the molecule of the active constituent of potato root diffusate.

Problems more comprehensive than trigger mechanisms were considered by E. J. Bell, C. A. Hopkins and M. R. Wyllie. These workers described their joint efforts to bridge the gap between the analytical and synthetic aspects of the *in vitro* culture of strigeid metacercariae to the sexually mature adult fluke. Media synthesized from chemically defined and simple constituents were very limited in their ability to promote growth and had to be assessed by sensitive criteria, such as cell-division, rather than by an increase in size of the organism or its parts. On the other hand, some of the unknowns of complex media which do support considerable growth could now be replaced by known substances, but the gap between the two approaches was still formidable.

Experiments which illustrate the differences that may exist between the metabolism of host and parasite were described by L. P. Joyner. Both sulphadimidine and pyrimethamine on their own showed therapeutic effect when administered to chicks infected with *Eimeria tenella*, but the two administered together gave more than additive effect. This is consistent with the theory that they antagonize different links in the same metabolic chain of the parasite, namely, the *p*-aminobenzoic acid – folic – folinic acid sequence. The drugs are also toxic to the chick, but when they were administered, together with the metabolites they are presumed to antagonize, differential reversal of their effects on host and parasite occurred.

Investigations into mechanisms concerning resistance of hosts to their parasites were reported by a number of speakers. F. W. Jennings presented the findings of a team of workers on immunity to *Dictyocaulus* infection in cattle. He showed that a double 'vaccination' of the host with irradiated infective larvæ protected it against further challenges of normal larvæ. L. Bailey dealt with the resistance of honeybees to epidemics of a range of parasites, and described how, without the aid of acquired immunity, the behaviour of the colony as a whole constituted a 'group immunity' reaction, and was successful in combating the disease as long as the community could develop normally. This was in part analogous to the dynamics of *Sarcoptes scabiei* infections in man, considered in two papers by K. Mellanby and W. N. Boog Watson, though in this case acquired immunity was an additional factor. The breakdown of resistance to infection in 'resistant' strains of potato by certain biotypes of potato root eelworm, and the investigation of its genetic basis in the nematode, was discussed by F. G. W. Jones. The evidence suggested a single locus for the effect, the double recessive conferring resistance-breaking, though the fact that some of the heterozygotes were resistance-breakers was against this simple interpretation.

The advantages of such a wide field at a conference of this kind were illustrated by the implications of the use of resistant species or strains to reduce the number of infective stages available to others that are susceptible. This is known to be valuable in the case of potato root eelworm, where resistant strains of the plant nevertheless stimulate hatching of the cysts, and was suggested by H. D. Crofton and P. G. Yonge as a mechanism in the control of *Diphyllobothrium* infections in trout when a normal proportion of coarse fish is present to reduce the level of infective material.

A plea to parasitologists not to lose sight of the economic aspect in the aims they set themselves when investigating the parasitic diseases of domestic animals was put forward by M. Christie. However, in the case of infections in man the parasitologist has a duty to assist in divesting him of his parasites. Contributions with this goal in mind included a mathematical analysis by W. E. Kershaw of the effects of parasitic infections on the mortality of insect vectors. These effects differed with the parasite and the vector, but the ability to support the parasite decreased with increasing age of the insect host, so that the vector may be present and yet incapable of transmitting the disease. Studies reported by A. I. Wright revealed an understandable, but nevertheless alarming, lack of knowledge of the etiology of hydatid disease on the part of some keepers of foxhounds in England, and showed that dogs fed on raw meat and offal readily become infected with *Echinococcus granulosus*.

No meeting of this kind would be complete without the description of a hitherto unknown animal. This was provided by J. Mahon, who presented studies on a new tapeworm, together with her reasons for placing it in the family Dilepididae.

P. A. G. Wilson

HORTICULTURAL AND FRUIT RESEARCH

The agricultural side of the work of the Agricultural and Horticultural Research Station at Long Ashton has been concerned mainly with fruit farming, but the retiring director, Prof. T. Wallace, had earlier described and photographed in colour the symptoms of numerous mineral deficiencies on a wide variety of crops. This raised so many questions that a research unit on plant nutrition was formed and is now firmly established at the Station under the ægis of the Agricultural Research Council. The annual report for 1957*, which was recently published, includes results of current work by this Unit on molybdenum deficiency, which has complex relations with nitrogen sources and with phosphate. A new type of symptom has indeed been produced when ammonium sulphate was used as a nitrogen source in place of nitrate. Other work of the Unit is outlined in the research summary of the report; much of it is obviously of a preparatory nature, but the results should ultimately provide knowledge upon an altogether new plane of detail for studies in plant nutrition.

In the main part of the report, C. Bould reports that two synthetic soil conditioners, HPAN (sodium salt, hydrolysed polyacrylonitrile) and VAMA (calcium salt, vinyl acetate maleic acid co-polymer), do indeed improve soil structure, but bring no increase in yield of strawberries. L. C. Luckwill and A. I. Campbell have obtained successful control of bindweed growing among black currant bushes by spraying 300 gal. per acre of 0·1 per cent potassium salt of 2 : 4 : 5-trichlorophenoxybutyric acid (2 : 4 : 5-TB). Long Ashton has undertaken the propagation of a virus-tested clone of loganberries, and E. W. Hobbis and A. I. Campbell have worked out a technique of leaf-bud propagation for its more rapid accomplishment. Barbara A. Rake reports that gooseberry cuttings taken from fruiting bushes root more easily than those taken from younger plants, and A. I. Campbell finds that crab *C* rootstocks are necessary to provide sufficient stem for cider-apple standards. The stem building stock Bulmer's Norman could also, however, be double worked satisfactorily upon a variety of rootstocks. D. Wilson finds that the prolific new pear variety, Bristol Cross, introduced by the Station in 1933, is almost completely male sterile, and should therefore be grown only with a pollinating variety, for example, Conference.

Plant pathology occupies a large part of the report. L. C. Luckwill has obtained evidence that 'chat fruit' disease of the apple Lord Lambourne is transmissible by graft and of virus origin. Spores of the fungi causing apple and pear scab diseases require a period of wetting before they will germinate, the so-called 'Mills periods'. Most of the work on these periods, which have forecast value, was done with ascospores of *Venturia inaequalis* (apple scab), but D. Wheatley shows that conidia of this fungus gave a higher percentage germination and grew more rapidly than ascospores. Conidia of *V. pirina* grew even faster than conidia of *V. inaequalis*, and these facts would necessitate a revaluation of Mills' forecast periods to meet particular situations, according to whether ascospore or conidial infection was involved. Several losses of stored apples have occurred in recent years; they are caused by the fungi *Gloeosporium perennans* and *G. album*, which infect the fruit while still on the tree. R. O. Sharples finds that the fungi complete their life-cycles as weak parasites on apple shoots, that fruit infection is incidental, and that spore production can be reduced by sprays or wound paints containing phenyl mercury chloride. R. T. Burchill shows that apple mildew, *Podosphaera leucotricha*, infects the buds via the petioles, a bud remaining susceptible to attack for about a month after emergence.

R. J. W. Byrde and Nora N. Waugh report laboratory tests of eleven new potential fungicidal materials. Three of them—*n*-dodecyl-guanidine acetate, 2 : 4-dichloro-6-(*o*-chloroanilino)-*s*-triazine, and *o*-hydroxydiphenyl—were selected for field tests. Bordeaux mixture is usually made by adding concentrated copper sulphate solution to diluted lime suspension, but E. Somers shows that better performance can be expected if the lime is concentrated and the copper sulphate dilute. R. J. W. Byrde, G. M. Clarke and C. W. Harper have again found in 1957 that captan used as a post-blossom spray on apples increased the incidence of mildew. J. T. Martin and J. A. Pickard have studied the retention of mercury salts by apple fruits after seven sprays with 0·003 per cent mercury as phenyl mercuric nitrate. A fruit weighing 200 gm. had about 10 µgm. of mercury: 2 µgm. in the peel, 8 µgm. in the flesh and less than 1 µgm. in the core. T. E. Cobbold describes a compressed air nozzle for small-volume spraying, and has also assessed the field performance of the power-knapsack type of mist sprayer. Little is known about the chemical composition of the cuticle in different plants, but J. T. Martin, R. F. Batt and Margaret F. Roberts show that there are considerable variations in the overall amounts of cuticle and in the proportions of wax and cutin between plants. As the cuticle is the initial receptor of sprays, a knowledge of its constitution should be important in practice.

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* University of Bristol. The Annual Report of the Agricultural and Horticultural Research Station (The National Fruit and Cider Institute), Long Ashton, Bristol, 1957, with Index 1953–57. Pp. 182 + 10 plates. (Long Ashton, Bristol: Agricultural and Horticultural Research Station, 1958.) 15*s*.

There are also papers on domestic food preservation, on fruit juices, and on the conversion and utilization of the Station's plantation of cricket bat willows. Research workers and advisory officers will find a most useful list of papers published by members of the Station's staff in 1957, and there is a further index of papers published in the Long Ashton annual reports during 1953–57. JOHN GRAINGER

INSECT RESISTANCE TO INSECTICIDES

THE discovery by Müller of the insecticidal properties of DDT in 1939 was followed by the introduction of a whole range of similarly powerful synthetic insecticides in the years immediately after the Second World War. These included other chlorohydrocarbons like dieldrin, the gamma isomer of benzene hexachloride, and a number of organophosphorus compounds. Their use marked a new era in the control of arthropod pests and the development of what is now an important branch of the chemical industry. The spectacular control of the malarial mosquito, for example, brought the global eradication of the disease within the realm of probability.

The development of insect resistance to some of these insecticides, however, now threatens to undermine much of the progress achieved and the hopes of some large-scale public health programmes in tropical latitudes especially. Resistance may attain such levels as to involve virtual immunity of the insect to an insecticide and the failure of effective control in the field. Yet remarkably little is known about the mechanisms of resistance and in no case has a satisfactory counter-measure been developed except to change to one of the dangerously few alternative insecticides. A major problem has been to engage the interest of suitably equipped and experienced workers and to facilitate the exchange of information and insect material between research workers and the often far-distant field entomologist or sanitarian. A good deal has recently been achieved by a small dedicated group of the World Health Organization in Geneva due in no small part to the tireless efforts of Prof. A. W. A. Brown. His recent monograph on "Insecticide Resistance in Arthropods"* is one result of a two-year term-of-office with the Organization and reflects an authority and erudition made possible only by a combination of the uniqueness of the author's position and his personal industry.

Four long chapters deal with the genetic nature and development of resistance, resistance in species which are vectors to man, what is known of the physiological and biochemical mechanisms of resistance, and resistance in species which are not vectors.

The first chapter describes the historical development of resistance in vector species, the public health implications, the genetic nature of the inheritance of resistance, and the important problem of detecting significant levels of resistance in field populations. The second chapter deals *seriatim* with case histories of the vectors such as body lice, and mosquitoes transmitting malaria and yellow fever. The third chapter deals mainly with the housefly, since much the larger part of systematic research has been conducted with this insect. The final chapter, like the second, deals with case histories of the field development of resistance in fruit flies, bed bugs and cockroaches.

The monograph will interest the geneticist as well as entomologist and biochemist. There is abundant evidence that resistance is a pre-adaptive phenomenon and under genetic control, so that the development of resistance to an insecticide is due to selective breeding from naturally resistant phenotypes. The easy culture of highly resistant strains in the laboratory has probably provided an unprecedented opportunity for studying the biochemistry and genetics of evolution.

Prof. Brown has wisely refrained from speculating about the future of the resistance problem and the possible development of countermeasures. These may indeed involve entirely new concepts in the field of insect control. On the other hand, there are grounds for believing that effective counter-measures can be developed on the basis of the continued use of insecticides: for example, the exploitation of enzymes which appear to be present in far higher concentrations in the tissues of a resistant insect than in a susceptible one, or the alternate use of insecticides negatively correlated in their respective toxicities towards susceptible and resistant strains.

Some readers may be disappointed to find relatively little reference to resistance of agricultural pests and its implications. For example, there is no mention of the serious levels of resistance to the chlorinated hydrocarbons, reported in 1957 to have developed in the cotton boll-weevil infesting the larger cotton-growing area of Louisiana. While such an omission is not surprising in a publication of the World Health Organization, it might have been usefully indicated in the title or in a sub-title of the monograph. Prof. Brown has, perhaps, drawn a little heavily on pre-publication material some of which has shown signs of being a little premature. These blemishes notwithstanding, the monograph is a timely and invaluable contribution to an appreciation of this big problem. It is recommended as salutary reading to all interested in the chemical control of arthropod pests and as an essential text to all concerned with the problem of resistance itself.

F. P. W. WINTERINGHAM

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* World Health Organization. Monograph Series No. 38: Insecticide Resistance in Arthropods. By Dr. A. W. A. Brown. Pp. 240. (Geneva: World Health Organization; London: H.M. Stationery Office, 1958.) 15 Swiss francs; 25*s*.; 5 dollars.

METABOLISM OF MYLERAN (1 : 4-DIMETHANESULPHONYLOXYBUTANE)

By Dr. J. J. ROBERTS and Dr. G. P. WARWICK

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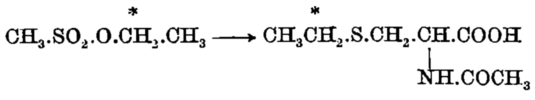
EARLIER publications[1,2] on the mode of action of biologically active alkylating agents described the presence of derivatives of S-alkylated cysteines in the urine of rats given alkyl alkanesulphonates by intraperitoneal injection. Thus, for example, 1-^{14}C-ethyl methanesulphonate (I) was shown to be excreted as N-acetyl-S-1-^{14}C-ethylcysteine (II) and other derivatives of S-1-^{14}C-ethylcysteine.



$$\mathrm{CH_3.SO_2.O.\overset{*}{C}H_2.CH_3 \longrightarrow CH_3\overset{*}{C}H_2.S.CH_2.\underset{\displaystyle NH.COCH_3}{\underset{|}{CH}}.COOH}$$

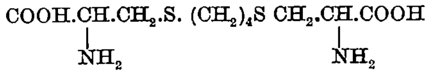
I II

This work was regarded as a prelude and guide to the investigation, now reported, of the *in vivo* reactions of 1 : 4-dimethanesulphonyloxybutane (myleran) (III) ; $n = 4$; a cytotoxic alkylating agent used clinically in the treatment of chronic granulocytic leukæmia[3]. These studies also provide a comparison between the *in vivo* reactions of two structurally related compounds, one monofunctional and the other bifunctional. Myleran is far more toxic to the rat than ethyl methanesulphonate and, unlike the latter, exerts a profound effect on the bone marrow, which results in a drop in the number of circulating neutrophils[4].

$$\mathrm{CH_3.SO_2.O\ (CH_2)_{\mathit{n}}.O.SO_2.CH_3}$$

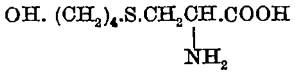
III

By analogy with ethyl methanesulphonate it was anticipated that myleran would react *in vivo* with the thiol group of cysteine or cysteine-containing compounds (peptides or proteins), resulting in the urinary excretion of metabolites of S-dicysteinylbutane (IV). However, evidence for such a reaction product was not obtained, while it was established that injected S-dicysteinylbutane was excreted in the free and conjugated forms. Furthermore, S-(4-hydroxybutyl)cysteine (V), which would be formed if one functional group of myleran reacted with cysteine while the other was hydrolysed, was also shown to be excreted as conjugates of sulphur compounds which were detectable on paper chromatograms. These compounds were not present on similarly prepared chromatograms of urine from rats which had received injections of myleran.



$$\mathrm{COOH.\underset{\displaystyle NH_2}{\underset{|}{CH}}.CH_2.S.\ (CH_2)_4S\ CH_2.\underset{\displaystyle NH_2}{\underset{|}{CH}}.COOH}$$

IV



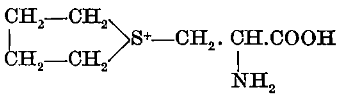
$$\mathrm{OH.\ (CH_2)_4.S.CH_2\underset{\displaystyle NH_2}{\underset{|}{CH}}.COOH}$$

V

After injection of 2 : 3-^{14}C-myleran (prepared by Dr. P. Brookes) into a male Wistar rat, only 4 per cent of the radioactivity was exhaled as carbon-14 dioxide during 24 hr. On the other hand, 2 : 3-^{14}C-1 : 4-butanediol, the hydrolysis product of myleran, was shown to be converted almost exclusively to carbon dioxide labelled with carbon-14 *in vivo*, indicating that myleran is not metabolized via this route. It will be recalled that conversion to carbon dioxide was one of the major routes of metabolism of ethyl methanesulphonate.

Autoradiographs of paper chromatograms of the urine collected during 24 hr. after injection of myleran revealed the presence of one major metabolite, which was stable to treatment with hot mineral acid and failed to give any positive test (on paper chromatograms) with a number of reagents such as ninhydrin or platinic iodide. The necessarily minute doses of myleran which were given to rats precluded isolation of adequate quantities of the metabolite for characterization.

In view of these apparent differences between the metabolism of ethyl methanesulphonate and myleran, the reaction between myleran and cysteine *in vitro* was studied in greater detail. Apart from the formation of some S-dicysteinylbutane and S-(4-hydroxybutyl)cysteine the major product of the reaction under a variety of conditions was the S-β-alanyltetrahydrothiophenium cation (VI).



VI

The ion was characterized as its picrate and was unambiguously synthesized by heating S-(4-hydroxybutyl)cysteine with concentrated hydrochloric acid.

The urine obtained from a rat which had been injected with this sulphonium salt (VI) (prepared from the labelled myleran) also contained one major metabolite identical with that formed from myleran, as judged by comparing autoradiographs of identically prepared paper chromatograms of the respective urines. The identity of this major metabolite has still to be determined ; but since it is no longer an amino-acid it is clearly a break-down product of the cyclic sulphonium ion (VI), possibly a derivative of tetrahydrothiophene. The sulphonium salt (VI) was shown to be labile in the presence of alkali and was converted to alanine by electrolytic reduction.

These results indicate that the predominant reaction which myleran undergoes in the rat is alkylation of a thiol group, and by analogy with ethyl methanesulphonate probably that of cysteine or cysteine-containing compounds, to give a cyclic sulphonium salt, which is the precursor of the major urinary metabolite.

Certain sulphonium ions have been shown to possess alkylating ability, depending both on the nature of substituents and the associated anion. However, the fact that S-dicysteinylbutane or S-(4-hydroxybutyl)cysteine is not produced when (VI) is treated with excess cysteine or water, and that it is not metabolized to these compounds *in vivo*, would suggest that this sulphonium ion is not an alkylating agent. This is supported by the fact that it was found to be non-toxic to the rat, and did not produce myleran-like effects on the bone marrow at a dose as high as 1 gm./kgm. body-weight (L. A. Elson, private communication). It seems likely, therefore, that this compound is not responsible for the pharmacological effects of myleran; but the possibility remains that the ion is unable to penetrate the necessary cell boundaries to produce its effects. Those pharmacological properties of myleran, therefore, which result from reaction with thiol groups are likely to be due to reaction with thiol groups of proteins or nucleoproteins leading to sulphonium ion formation. The formation of such ions may offer an explanation for the differences in pharmacological properties which have been observed between myleran and its monofunctional counterpart, ethyl methanesulphonate. While both compounds have been shown to react with thiol groups *in vivo*, the formation of sulphonium ions from myleran may have more far-reaching effects by modifying the structure and function of macromolecules. It has also been found that in the series of *bis*-methanesulphonyloxy esters[4] (III; $n = 2$–10) maximum toxicity and maximum activity against the neutrophils occur when $n = 4$ or 5, distances which would permit a facile cyclization to five- or six-membered rings, respectively[5]. This view is supported by some preliminary *in vitro* chemical studies of the reaction between cysteine and various members of the series (III; $n = 3$, 5 and 6).

Other alkylating agents such as the sulphur and nitrogen mustards could conceivably undergo *in vivo* ring formation in an analogous manner and work is in progress to determine whether this is the case.

This work has been supported by grants to the Chester Beatty Research Institute (Institute of Cancer Research, Royal Cancer Hospital) from the British Empire Cancer Campaign, the Jane Coffin Childs Memorial Fund for Medical Research, the Anna Fuller Fund and the National Cancer Institute of the National Institutes of Health, U.S. Public Health Service. We wish to thank Prof. A. Haddow and Dr. L. A. Elson for their interest in the work, and to record our appreciation for helpful discussion with many of our colleagues. We should also like to acknowledge technical assistance from Miss M. Morton and Miss M. Gill.

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WEAL AND FLARE IN HUMAN SKIN PRODUCED BY HISTAMINE AND OTHER SUBSTANCES

By Dr. A. HERXHEIMER and Dr. M. SCHACHTER

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ALTHOUGH histamine is the most prominent wealing agent in man, evidence is accumulating which indicates that other naturally occurring substances have a similar action on capillary permeability. Among substances that have been found to have this property in laboratory animals are kallikrein[1,2], kallidin, bradykinin, wasp kinin[3] and 5-hydroxytryptamine[4]. The present experiments demonstrate that wasp kinin, kallidin, bradykinin and kallikrein preparations are effective wealing agents in man on intradermal injection. Also, that the size of flare and the size of weal produced by these substances do not run parallel. For example, kallikrein, which increased capillary permeability, produced no flare, whereas 5-hydroxytryptamine, which was an effective flaring agent, failed to cause wealing or other evidence of increased capillary permeability. Until pure substances are available the possibility exists that the permeability-enhancing agents in our preparations are not identical with the smooth muscle contracting (kinin, kallidin, bradykinin) or vasodilator (kallikrein) principles.

Four healthy men, aged 20–23 years, were injected intravenously with 10 ml. of a 5 per cent sterile solution of Evans blue in saline. Intradermal injections (0·05 or 0·1 ml.) of the test substances in saline were made into the skin of the back 30 min. later, and flares and weals were measured 8–15 min. after injection. Measurements were made either directly on the subject or from projected coloured photographs. The mean of the largest diameter and that at right angles to it was taken as the size of the flare or weal; the flare measurement included the diameter of the weal. Serial photographs of the skin reactions indicated that the flare usually reached its maximum in 4 min. and was beginning to fade in 15 min. The weal reached its maximum size in 9 min. and remained so beyond 30 min. Reactions were measured, therefore, 8–15 min. after the intradermal injection. Small weals that were not blue were designated as 0 or 0–4, since they presumably represent injected fluid and not fluid which had left the circulation. These were never, in any event, greater than 4–5 mm. in diameter.

Wasp kinin was prepared by extraction of wasp glands with glacial acetic acid, precipitation with ether, and repeated washing of the precipitate with ethanol. This preparation contained 1 unit in 0·4 μgm. of freeze-dried material. Kallidin and bradykinin were prepared by the action of human salivary kallikrein or trypsin, respectively, on heated ox globulin. These preparations were of equal potency and contained 1 unit in 75 μgm. dry material in terms of the unit of Rocha e Silva, Beraldo and Rosenfeld[5].

Details of the units and preparation of these different substances are given by Holdstock *et al.*[3]. Kallikrein was prepared from the saliva of the subject in whom it was eventually tested. There is as yet no standard of kallikrein in terms of its ability to release kallidin ; the preparation used in these experiments, however, released detectable amounts of kallidin when incubated with heated human plasma in concentrations of 10 µgm./ml. or less.

The results obtained with intradermal injections of 0·05 ml. kinin, histamine and 5-hydroxytryptamine in three subjects are shown in Table 1. Histamine and partially purified wasp kinin produced marked blueing with a large surrounding flare and were approximately equi-active on a weight basis. 5-Hydroxytryptamine produced a flare, but no blueing, even in much higher concentrations. The small, evanescent flare produced by saline was not measurable 5 min. after the injection.

Preparations of bradykinin and kallidin which were of equal activity on the guinea pig ileum were compared with kallikrein, histamine, kinin and 5-hydroxytryptamine in a fourth subject (Table 2). In this experiment, a greater volume, namely, 0·1 ml., of each solution was injected. Kallidin and bradykinin were effective blueing agents but much less active in producing flare. Thus, unlike histamine and wasp kinin (Table 1), they were still producing blueing reactions without an associated flare in high dilutions. Kallikrein, which produced larger weals, was also practically devoid of flaring properties in the concentrations used. 5-Hydroxytryptamine, on the contrary, again elicited a strong flare but no blueing reaction.

Table 1. FLARE AND WEAL PRODUCED BY INTRADERMAL INJECTIONS (0·05 ML.) OF KININ, HISTAMINE AND 5-HYDROXYTRYPTAMINE
(Combined results from three subjects)

Substance	Concentration (µgm./ml.)	Mean diameter (mm.)	
		Flare	Weal (blue area)
Wasp kinin	500	48, 44, 43	15, 14, 10
	50	48, 44, 35	13, 10, 9
	5	32	9
Histamine	500	55, 51	16, 14
	100	47	13
	50	48, 41	10, 10
	10	43	9
	1	30	9
5-Hydroxytryptamine	2,500	35, 32	0–4, 0–4
Isotonic saline		0, 0	0–4, 0–4

Table 2. FLARE AND WEAL PRODUCED BY INTRADERMAL INJECTIONS (0·1 ML.) OF BRADYKININ, KALLIDIN, KALLIKREIN, HISTAMINE AND 5-HYDROXYTRYPTAMINE IN A FOURTH SUBJECT

Substance	Concentration (µgm./ml.)	Mean diameter (mm.)	
		Flare	Weal (blued area)
Bradykinin	1,000	30	15
	333	27	13
	100	0	12
	10	0	10
Kallidin	1,000	28	15
	333	20	9
	100	0	11
	10	0	9
Kallikrein	500	trace	18
	50	0	15
Kinin	100	52	18
Histamine	100	58	20
5-Hydroxytryptamine	100	34	0–4
Isotonic saline		0	0–4

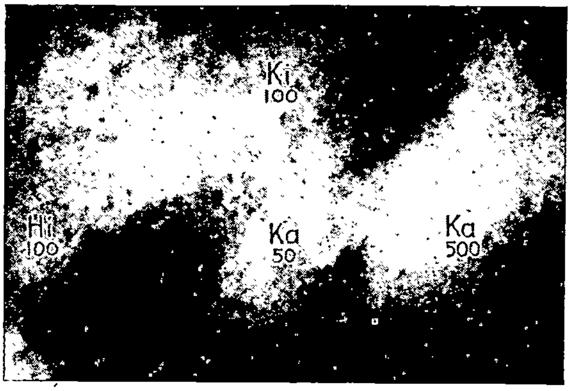

Fig. 1. Photograph of weal and flare reactions of human skin to intradermal injections of 0·1 ml. of histamine (*Hi*), wasp kinin (*Ki*) and salivary kallikrein (*Ka*). The numbers represent the concentration of the solutions in µgm./ml. The subject had received Evans blue solution previously, and the blue weal is the dark central area surrounded by the lighter flare. Note the complete absence of flare with kallikrein

Fig. 1 shows the flare and weal produced by histamine and wasp kinin contrasted with the pure wealing action of kallikrein.

These results indicate that in addition to histamine a number of naturally occurring substances produce wealing in man. They include wasp kinin, salivary kallikrein, kallidin and bradykinin. 5-Hydroxytryptamine, which increases capillary permeability in rat skin[4,6], has no such effect in man, where, however, it is effective in producing the local flare reaction. It is very unlikely, therefore, that the release of 5-hydroxytryptamine is of significance in reactions involving wealing or angio-œdema in man.

The fact that salivary kallikrein and the polypeptide, kallidin, which it releases are effective in increasing capillary permeability is of interest, because plasma contains large amounts of kallikrein in an inactive but activable form[7]. Indeed, there is a suggestive similarity in the blueing of skin produced by salivary kallikrein in our experiments and that produced by diluted human plasma in man[8]. In both instances flare reactions were strikingly absent. It may well be, therefore, that the agent in diluted human plasma which increases permeability is kallikrein, since there is also evidence that dilution of plasma or serum activates kallikreinogen, the precursor of serum kallikrein[9].

In our experiments kallidin itself did produce some flare reaction, although this was much less prominent than with histamine, kinin, or 5-hydroxytryptamine. In higher dilutions kallidin no longer produced any flare although it still caused blueing. Our preparations of kallidin and bradykinin are quite impure, and until pure preparations are available for testing, it will be impossible to say whether the mild flare reaction is produced by the same substance which produces the increase in capillary permeability.

This work was in part financed by a grant from the Central Research Fund of the University of London to one of us (M. S.), which gratefully is acknowledged.

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CELLULOSE ACETATE AS A MEDIUM FOR IMMUNO-DIFFUSION

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A NUMBER of well-established methods for demonstrating antibody–antigen reactions depend on the formation of precipitin lines by diffusion through a jelly—usually agar. Some of the difficulties associated with the use of jelly would be avoided if the diffusion process could occur in a sheet of solid material. For satisfactory results such a material would have to be wettable, allow the free diffusion of large molecules without adsorption, have a uniform composition and be readily available. We have found that cellulose acetate membrane (Oxo, Ltd.) fulfils these requirements and is equal, if not superior, to agar jelly for immuno-diffusion purposes. This material, in strip form, was introduced by Kohn[1] for electrophoresis and was later developed, in conjunction with agar, for immuno-electrophoresis[2,3].

For the Ouchterlony–Elek double-diffusion method, pieces of suitable size are cut from a membrane strip or, alternatively, unprinted circular membrane filters may be used. The positions where the samples are to be applied are marked lightly with non-diffusing ink (for example, with a ball-point pen). The membrane is then soaked in the desired buffer solution, blotted lightly so that no excess moisture is visible and supported in a horizontal position in a moist chamber. (A suitable support consists of pins with their heads pressed into a 'Plasticine' base so that the points are uppermost.) By means of capillary tubes, small amounts (1–5 μl.) of the samples are applied as spots or lines to the membrane surface. Antigen and antiserum are usually placed 1 cm. apart, but the arrangement and distance may be chosen as required. The membrane is allowed to remain in the moist chamber until the drops have sunk into the surface, following which it is immersed in a bath of liquid paraffin or 'Whitemor 120' oil (Manchester Oil Refinery Co.). Diffusion occurs in the moist membrane and the formation of precipitin lines is usually complete in 2 days at room temperature. Excess of oil is wiped off, and the remaining oil removed by a quick wash in ether or light petroleum. Thereafter, water-soluble material is removed by soaking in saline or buffered saline solution for 1–3 hr. with occasional agitation. The membrane is then blotted and stained to render the precipitin lines visible and finally dried flat between filter paper sheets at room temperature. The stains used were ponceau *S* (G. T. Gurr) (0·15 per cent in 3 per cent trichloracetic acid) for strong precipitin lines and dilute nigrosine *WS* (0·001–0·0025 per cent in 2 per cent acetic acid) for weaker lines as described by Kohn[3]. The membrane may be stained first with ponceau then with nigrosine. Examples of double diffusion on membranes are illustrated in Figs. 1*a* and 2*a*. Fig. 1*b* shows a conventional agar plate diffusion employing the same samples of antiserum and antigens as in Fig. 1*a*.

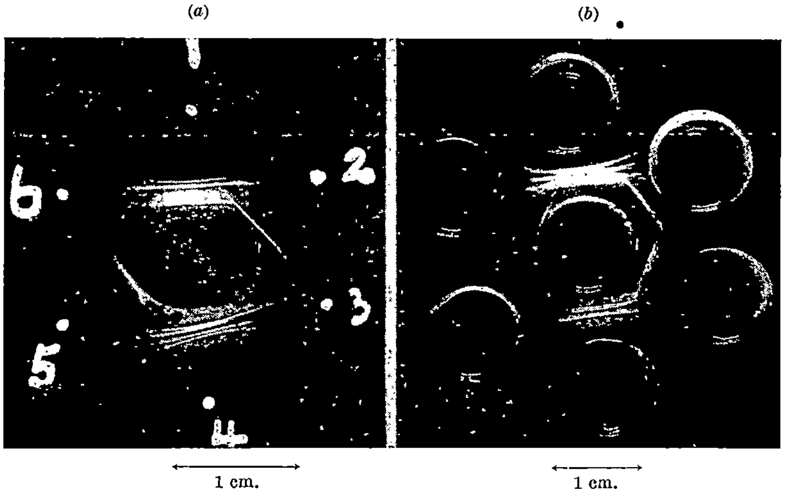

Fig. 1. (*a*) Double diffusion on cellulose acetate membrane at *p*H 7 for 2 days. Human serum or human serum fractions (2–3 μl.) placed at positions 1–6, horse anti-human serum at centre. Stained with ponceau *S*. Negative print from oil transparency. (*b*) Diffusion on agar with same samples (about 0·3 ml. in each well)

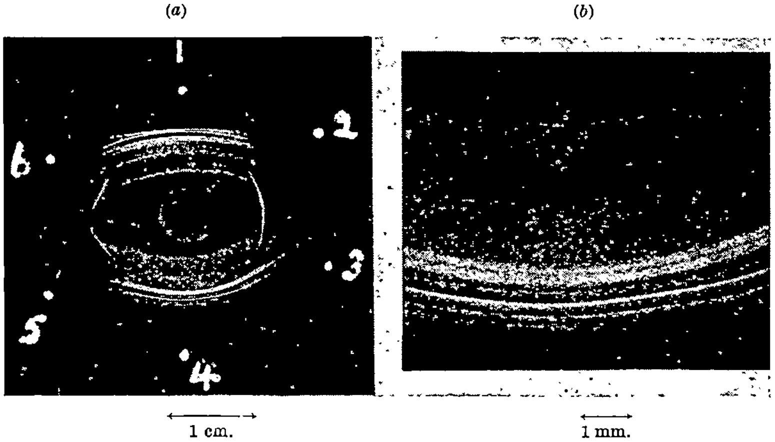

Fig. 2. (*a*) Diffusion on cellulose acetate at *p*H 8·6. Horse anti-human serum at centre. Normal human sera at positions 1 and 4. Concentrated urines from cases of myeloma at positions 2, 3, 5, 6. Stained with ponceau *S*. (*b*) Portion of membrane above position 4 in (*a*) enlarged direct from transparency

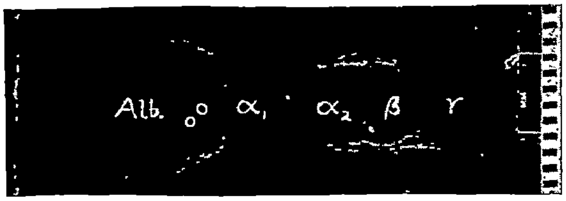

Fig. 3. Immuno-electrophoresis on cellulose acetate membrane (12 cm. × 2½ cm.). Electrophoresis of normal human serum (3 μl.) carried out at 20 V./cm. for 1½ hr. in barbitone buffer, *p*H 8·6. Horse anti-human serum placed along membrane above and below antigens after electrophoresis. Stained with nigrosine. Negative print from transparency

The stained membrane is best viewed in transmitted light, and may be photographed in this way. However, when soaked in 'Whitemor' oil, cellulose acetate, when dry, becomes almost transparent. The oiled, stained membrane if sandwiched between glass plates may then be used as a transparency for projection or for enlargement in a photographic enlarger. An enlargement of a small portion of a membrane is shown in Fig. 2*b* and demonstrates the fine nature and sharpness of the precipitin lines.

The Oudin-type of diffusion is carried out on a strip of cellulose acetate. Antigen and antiserum are each applied across the width of the strip about ½ in. apart. The strip is hung vertically in the oil during the diffusion stage.

For immuno-electrophoresis, the electrophoresis stage is carried out on the membrane strip as described by Kohn[1,3], the sample (1–5 μl.) being applied as a drop or across a short line at the starting position. After the electrophoresis, and without removing the strip from the box, a line of antiserum is applied from the capillary, preferably in one movement, parallel to the electrophoresis direction and at a distance of 0·5–1 cm. from the antigens. The lid is then replaced until the serum has soaked in, when the strip is removed to the oil bath. Subsequent procedures are as described above. Fig. 3 illustrates an immuno-electrophoretic pattern.

In these experiments diffusion under oil has been preferred to diffusion in a moist atmosphere, because in the latter conditions it is difficult during a long period to avoid unequal evaporation from the membrane surface which might cause artefact or distorted lines. The inert oil does not appear to have any denaturating effect on proteins.

Certain precautions should be observed in these techniques. No portion of the membrane should be allowed to become dry before transference to the oil bath. Should this occur, the membrane can be returned to the moist chamber and exposed until uniformly damp. All solutions and samples should be free from particulate matter, and the former should preferably contain a preservative to prevent bacterial growth; colonies of micro-organisms may cause distortion of precipitin lines and form an undesirable patchy background when stained. Membranes should be handled with forceps.

Cellulose acetate membranes have a number of advantages over agar. The material is relatively simple to use and satisfactory results are obtained with about 1/100 of the amounts usually used for gel diffusion (Fig. 1). In a membrane, precipitin lines can occur at the position of application of the samples but cannot form in the wells of an agar plate (Fig. 1). There is no difficulty in storing membranes. In jelly, of course, formation of the precipitin lines can be seen directly, whereas in a membrane they are not visible until stained. However, replicate diffusions may readily be carried out on membranes to establish optimum conditions, and, moreover, the material can be treated with a variety of dyes and reagents to obtain information about the chemical nature of the antigen in the precipitin lines. Cellulose acetate membranes are manufactured of standardized material in Britain, but a cellulose nitrate membrane has been found to be satisfactory for diffusion though not for electrophoresis. It is probable that other existing membranes may also prove suitable for one or both purposes.

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ABSORPTION OF ALKALI CATIONS BY PLANT TISSUE CULTURES

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It was observed by Steward and Millar[1] that actively growing carrot and artichoke tissue cultures absorbed cæsium ions more slowly per unit of fresh weight than did slowly growing cultures, and they concluded that, in general, the rate of uptake of salt is more rapid in vacuolated than in meristematic cells.

There were certain features of the experimental procedure which make it difficult to be sure that the differences observed were really due to the different physiological condition of the two types of tissue culture, as Steward and Millar suggested. Another possibility which occurred to us is that differences in the ionic composition of the two media employed may have been responsible for the effect. Although the concentrations of cæsium ions supplied were the same for each tissue (10^{-3} *M* and 10^{-5} *M*), the media were different with respect to the concentration of other ions because of the addition of 10 or 15 per cent coconut milk as a stimulant to the rapidly growing cultures. A sample of coconut milk which we analysed recently contained about 0·045 *M* potassium and 0·015 *M* sodium. The medium in which the slowly growing tissues were cultured contained about 0·0017 *M* potassium and 0·003 *M* sodium, and so it is evident that the composition of the two media, at least with respect to these ions, was quite different. Now it is well known that alkali cations compete with one another for absorption by plant tissues[2–4], and consequently it is to be expected that uptake of cæsium would be depressed by the presence of potassium and sodium; and to the greatest extent in the actively growing cultures where the concentrations of potassium and sodium in the medium were highest.

In order to test this possibility, we have repeated some of Steward and Millar's experiments using carrot explants placed in media with and without 10 per cent coconut milk, but with the initial potassium

Table 1. Cæsium Content (μequiv. per gm. fresh weight), and the Fresh Weight (gm.) of 3 Replicate Batches of 10 Cultures of (*A*) slowly growing and (*B*) actively growing Carrot Tissues, after 2 and 3 weeks at 23° C.

Treatment		After 2 weeks Fresh wt.	 Cs content	After 3 weeks Fresh wt.	 Cs content
	1	0·086	1·3	0·147	1·4
A	2	0·098	1·1	0·137	1·7
	3	0·083	1·5	0·121	1·7
	1	0·240	0·76	0·560	0·51
B	2	0·245	0·66	0·608	0·52
	3	0·245	0·80	0·576	0·51

and sodium concentrations adjusted to the same value in both media (0·01 *M* for each ion) by addition of appropriate amounts of potassium and sodium chlorides. Cæsium chloride, labelled with cæsium-134, was supplied in each solution at a concentration of 10^{-4} *M*. The results obtained are shown in Table 1.

It was observed that although the actively growing cells absorbed more cæsium per culture than the slowly growing tissues, they absorbed considerably less on a gm. fresh weight basis. The differences observed were much lower than those found by Steward and Millar, who reported a 14-fold difference in uptake per unit of fresh weight between the two kinds of cultures. It must be concluded that the bulk of the effect observed by these workers is attributable to the composition of the media they used, rather than to the differing absorptive abilities of rapidly growing and slowly growing tissues; nevertheless the growing cultures seemed in our experiment to be somewhat inferior in their accumulatory capacity.

It seemed to us important to establish that the last conclusion is a general one, applying to physiologically important cations as well as to cæsium. Therefore, in another similar experiment we measured the uptake of potassium and sodium ions by carrot tissues grown in culture media containing each of these ions at a concentration of 0·01 *M* in the presence and absence of coconut milk.

Table 2. Potassium (K) and Sodium (Na) Content (μequiv. per gm. fresh weight), and the Fresh Weights (gm.) of (*A*) slowly growing and (*B*) actively growing Carrot Tissue Cultures, in 2 and 3 weeks at 23° C.

	After 2 weeks		After 3 weeks	
	A	*B*	*A*	*B*
	(*S.E.*)	(*S.E.*)	(*S.E.*)	(*S.E.*)
Fresh wt.	0·075 ± 0·006	0·262 ± 0·018	0·103 ± 0·006	0·536 ± 0·005
K	104 ± 7·8	123 ± 5·0	128 ± 12·1	123 ± 3·7
Na	68 ± 7·1	15·6 ± 1·0	70 ± 4·7	21·5 ± 1·1
Ratio K/Na.	1·5	7·9	1·8	5·7

The results of this experiment (Table 2) show that untake of potassium per gm. fresh weight was not significantly different between the two treatments. Uptake of sodium, however, was considerably higher in the slowly growing than in the actively growing tissues. The ratio K/Na in the tissue remained fairly constant over the experimental period in the case of slowly growing tissues, but decreased with time in the actively growing cultures. It is clear from these results that actively growing cells exhibit a stronger preference for potassium over sodium than do slowly growing ones, but that the difference becomes less marked with time. One possible explanation is that in actively growing tissues, containing a higher proportion of meristematic and nearly meristematic cells, relatively more of the absorbed ions are retained by the cytoplasm than in the slowly growing, mainly vacuolated cells where the bulk of the salt is transferred to the vacuoles. Retention in the cytoplasm may depend to some extent on ion-binding to specific sites (for example, on enzymes) which exhibit a marked potassium preference, whereas vacuolar accumulation in carrot cells may be relatively unselective with respect to sodium and potassium. In support of the last statement we have found that the prolonged metabolic accumulation of cations by washed slices of dormant carrot tissues, which is presumably mainly vacuolar accumulation, does not exhibit any marked discrimination between potassium and sodium. By the end of 3 weeks culture, the rate of growth in the actively growing tissue was beginning to decrease, and this was probably accompanied by increased vacuolation, which may account for the reduction in the ratio K/Na absorbed with time.

In an attempt to distinguish more clearly between cytoplasmic and vacuolar accumulation in tissue culture cells, we have studied the uptake of potassium and sodium by growing red beet cells in which it is already known that vacuolar accumulation exhibits a preference for sodium over potassium[4]. Explants were cultured in three different media: (*A*) a basal medium containing salts and sugar; (*B*) basal medium + indole-3-acetic acid (5×10^{-5} *M*); (*C*) basal medium + 10 per cent coconut milk. In all treatments the concentrations of potassium and sodium were adjusted initially to 0·01 *M*. The tissues grew appreciably during the experimental period although not so rapidly as carrot tissue cultures. Microscopic examination indicated that the growth in *A* and *B* was mainly, if not entirely, by cell enlargement; whereas the growth in *C* was predominantly the result of cell division accompanied by a little cell expansion.

Table 3. Potassium (K) and Sodium (Na) Uptake (μequiv. per gm. fresh weight) and the Fresh Weights (gm.) of Beet Tissues after 2 weeks of Culture at 23° C. in (*A*) Basal Medium; (*B*) Basal Medium + Indole-3-acetic acid; (*C*) Basal Medium + Coconut Milk

		A	*B*	*C*
Fresh wt.		0·044	0·081	0·079
Uptake	K	17	26	79
	Na	161	126	94
Ratio K/Na		0·11	0·21	0·84

Salt analyses showed (Table 3) that tissues in the various media absorbed sodium in excess of potassium during the experimental period. Tissues in the medium containing coconut milk, however, showed a much smaller preference than did the tissues cultured in the other media, and this might be attributable to a partial masking of the sodium-preferring vacuolar accumulation by concomitant cytoplasmic accumulation exhibiting a preference for potassium.

These results, therefore, are consistent with the idea of a two-phase metabolic accumulation of cations into: (*a*) cytoplasm and (*b*) vacuoles of plant cells. In both beet and carrot tissue cultures the two components could be distinguished on the basis of selectivity, and it is of interest that cytoplasmic accumulation apparently exhibited a potassium preference even when vacuolar secretion was characterized by a strong preference for sodium. Possibly this is related to the metabolic utilization of potassium rather than sodium by the cells.

A full account of this work, which is now being extended, will be published elsewhere in due course.

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LETTERS TO THE EDITORS

PHYSIOLOGY and BIOCHEMISTRY

The Work Output of Animals: Flight by Birds and by Man-power

MEN have always wanted to fly by their own power, like birds. But man is five times heavier than the heaviest flying creature of this or any other epoch. This creates difficulties; for as birds increase in size, their wing area diminishes in relation to their weight, since geometrical configuration and density remain roughly the same. This effect can only be countered by a greater expenditure of mechanical power by the larger specimens. In fact, the power required for level flight increases as $(\text{weight})^{1\cdot167}$ (Nonweiler, 1957, private communication).

Imagine a set of flying machines having the same shape and density, but differing in size. Let L be a characteristic length, and let V be the forward speed: then both lift and drag are proportional to V^2L^2. To achieve flight, weight = lift. Thus $L^3 \propto V^2L^2$, so that $V \propto L^{0\cdot5}$. Power expended = speed × drag $\propto V.V^2.L^2 \propto L^{3\cdot5} \propto (\text{weight})^{1\cdot167}$.

Successful aeroplanes have been built that range in size from a few grams up to nearly 200 tons. This is possible because artificial sources of power are available which provide considerably more power than is needed merely to achieve flight. Internal-combustion aero-engines are available with a weight range of $1:10^5$, and they all produce about 1·5 horsepower per kilogram. Full-sized engines actually become more powerful as they become bigger; their power goes up roughly as their $(\text{weight})^{1\cdot28}$.

But what of living creatures? What is their power output, and how does it vary with their size?

The Power Output of Animals is small compared with that of petrol engines of similar weight. For example, the maximum continuous power output of an athletic man is only 0·5 per cent of the output of an engine of comparable weight.

One of the best-established facts of comparative physiology is that the resting metabolism of animals varies with their size in an exceedingly regular manner. The smaller the animal, the greater its resting metabolism per kilogram. This is illustrated in line A of Fig. 1. The black spots represent actual measurements of the resting energy output of dogs, men, and horses. They are extracted from the much larger series of measurements on mammals and birds (from mice to elephants, a range in weight of more than five decades) collected by Brody (ref. 1, pp. 370, 388). He showed that these measurements could be fitted by the equation:

resting metabolism in h.p. = $4\cdot6 \times 10^{-3}$ (weight in kgm.)$^{0\cdot734}$

Line A is drawn from this equation.

Now, an animal at rest is doing no external work, its energy output is all in the form of heat. We want to know what happens when it *is* performing external mechanical work. This is not easy to investigate experimentally. Most animals can be lulled to rest, but few can be induced to work steadily and energetically. Moreover, the mechanical work must be performed in such a way that it can be measured. The final difficulty, which is almost psychological, is that a valid comparison can only be made between animals that are trying equally hard to perform comparable tasks.

The only measurements that I have been able to find in which all these criteria were satisfied were on dogs climbing a treadmill[2] or pulling a sledge[3]; men cycling, rowing, climbing, etc; and horses pulling[1].

In each case it is possible to fit a reasonably good straight line to the points which is parallel with line A. This shows that the output of mechanical work varies with size in exactly the same way as does the resting metabolism, and helps to support Brody's claim that one can express the effort that an animal is exerting as a multiple of its resting metabolism. Lines B, C and D correspond to mechanical power outputs of 1·7, 4·8 and 25 times basal heat production. Because of the relative inefficiency of muscular contraction, the total production of energy (work + heat) resulting from exercise will be about four times greater, say, 7, 20 and 100 times basal. The conclusion to be drawn is that the maximum metabolic rate is linked to the resting metabolic rate; though it is not clear what the physiological mechanism of this link may be.

We are now in a position to appreciate the dilemma of the birds that tended, in the course of evolution,

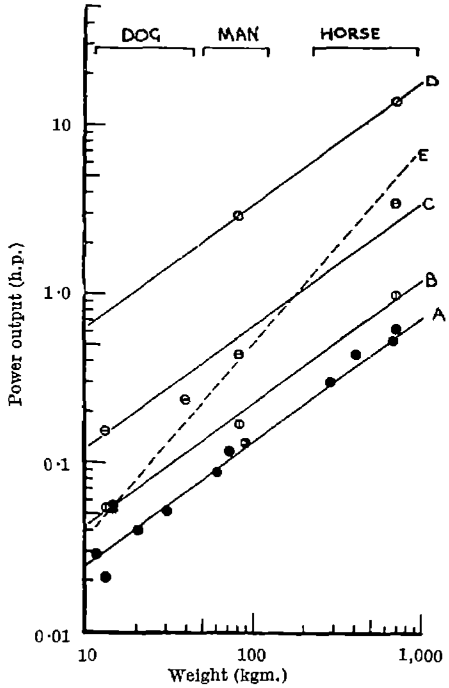

Fig. 1. Power output of animals as a function of body-weight; plotted on a double logarithmic scale. A (black spots), heat output at rest; B, C, D (circles), work output at various levels of effort; B, maintained all day; C, maximum steady-state (maintained 5–30 min. approximately); D, brief effort (maintained a few seconds only, by going increasingly into oxygen debt). The full lines have been fitted from the equation: horse-power = const. 10^{-3} (kgm.)$^{0\cdot734}$, where const. is 4·6, 7·4, 21 and 113 respectively; E (dashed line) shows the power required to fly, calculated from the relation:

$$\text{horse-power} = 2\cdot33 \times 10^{-3}\,(\text{kgm.})^{1\cdot167}.$$

* Intersection of B and E represents the great bustard.

to become larger. As they did so their power production (lines *B*, *C*, *D*) became relatively less, while their power requirement (line *E*) increased. Evidently flying ceased to be a practical proposition for birds heavier than about 15 kgm. This is not to say that it is impossible; merely that it is too expensive a means of transportation for a bird in a competitive world.

Line *E* has been drawn with the theoretical slope derived from the relation:

$$(\text{power required}) = \text{const. } (\text{weight})^{1\cdot167}$$

but in order to fix the position of the line it is obviously necessary to estimate the value of the constant. This involves estimating, or guessing, the power output of a bird of known weight. I have chosen the great bustard, because, at 14·5 kgm. it is the heaviest flying bird. It is said to be capable of powerful and sustained flight, so I have assumed that it can fly with its 'all-day' level of effort (line *B*) and have accordingly made line *E* intersect *B* at 14·5 kgm.

Fig. 1 then leads to the interesting conclusion that it should be possible for birds weighing up to 170 kgm. to fly while still remaining in oxygen balance, though they would have to work extremely hard to do so. Line *E* passes just below the maximum steady-state point for a man; so if he had wings he would be able to fly. Unfortunately, in practice, flying machinery will have to be carried as an extra—the extra weight per man (assuming a two-man machine) can scarcely be less than 40 kgm. This may mean that man can only fly by incurring an oxygen debt, which would limit the performance to a few minutes.

These conclusions, based on comparative and dimensional grounds, entirely agree with those of Nonweiler[4], who has calculated in a purely aerodynamic design-study the power needed for flight by a suitable aircraft, and compared this with the known power output of man. They disagree with the conclusions of Günther and Guerra[5], who assumed in their calculations that the power required for flight increased as $(\text{weight})^{0\cdot667}$.

Calculation thus indicates that practical man-powered flight is possible, but only just possible, so that good engineering will be needed to achieve it. Clearly, the matter should be put to experimental test.

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Fast and Slow Muscles in Mammals

THE histology and physiology of both fast and slow types of cat striated muscle were studied in detail by Denny-Brown[1]. He reported that the histological appearance did not distinguish definitely between the functionally fast and functionally slow type of muscle fibre. From his physiological investigations he concluded that the typically fast muscles (for example, gastrocnemius) were specialized for phasic contractions, whereas the typically slow muscles (for example, soleus) were utilized for tonic contractions. He suggested that a comparable arrangement of fast gastrocnemius and slow soleus might be found in many animals, including man.

The renewed interest in the physiology of fast and slow contracting muscles[2] has prompted an attempt to measure the contraction times in human muscles. The responses of the gastrocnemius and soleus muscles were examined in sixteen normal males between the ages of 18 and 40 years, some repeatedly. The subjects were examined while lying at rest in the prone positions. The muscle contraction was recorded by means of a saline-filled needle inserted into the belly of the muscle and connected to a capacitance manometer measuring the pressure among the fibres. The muscle fibres lying adjacent to the recording needle were caused to contract by an electrical stimulus applied either via the recording needle itself, or via a second needle placed in close proximity to the first. Thus the pressure changes within a group of contracting muscle fibres were measured. When this technique was used in the muscles of the cat and the results compared with simultaneous measurements of tension changes using the conventional strain gauge, it was found that, although it did not accurately record the time-course of the contractile process, nevertheless the method adequately differentiated the fast and slow muscles of the cat as shown in Fig. 1.

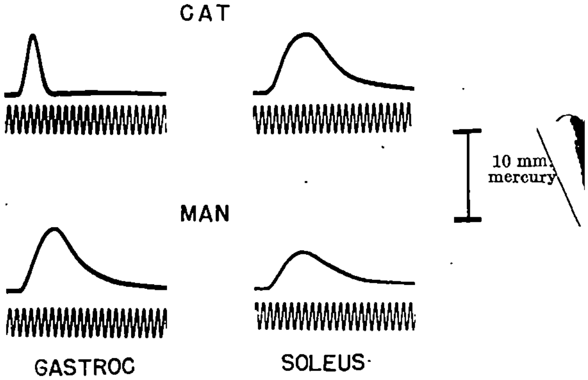

Fig. 1. Top row: Records obtained with a capacitance manometer of the pressure among a group of contracting fibres of gastrocnemius muscle (time to peak, 35 msec.) and soleus muscle (time to peak, 110 msec.) of the cat. Bottom row: Records obtained by similar recording from a human subject. Time, 50 c./s. Pressure, 10 mm. mercury

In the human subjects, no such clear-cut distinction could be made between the times of contraction of gastrocnemius and soleus. While the average time to peak of gastrocnemius contractions (110 msec., range 92–150 msec.) was somewhat shorter than that of soleus (120 msec., range 100–150 msec.), no regular pattern emerged, and in any one subject the times of contraction of the two muscles often differed by less than 20 msec.

In preliminary studies of human muscles other than those of the calf (forearm and hand), it was noted that considerably shorter times of contraction than with soleus and gastrocnemius could be obtained, but so far none shorter than 45 msec. to peak.

It therefore appears that, contrary to Denny-Brown's suggestion, the clear-cut differentiation of gastrocnemius and soleus into fast- and slow-contracting muscles respectively does not occur in the human.

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Effect of Monofluorosulphonate, Difluorophosphate and Fluoroborate Ions on the Iodine Uptake of the Thyroid Gland

Several inorganic anions have been found to interfere with the normal function of the thyroid gland[1-3], the perchlorate and thiocyanate ions being outstanding in this group. On the other hand, it has been shown that other common anions, including chloride, bromide, fluoride, sulphate, phosphate and bromate ions, have no significant effect on the iodine uptake and retention in the gland. The effect of perchlorate ions suggests a competition for some sites in the thyroid[1]. This assumption is supported by the fact that perchlorate ions concentrate in the gland[4]. Further, it was shown[4] that perchlorate ions do not undergo metabolization, thus excluding the possibility that they are involved in some enzymatic redox system. This behaviour of the perchlorate ion distinguishes it from other inorganic thyroid blocking agents like thiocyanate ions which have been shown to be metabolized and not to accumulate in the gland[2]. It occurred to us that the competition between perchlorate and iodide ions may be due to their similar monovalency and size. It is hard to compare the size of a spherical ion like iodide with that of a tetrahedral complex ion like perchlorate. Still we may compare the calculated volumes. The volume of ClO_4^- may be calculated taking $r(O^=) = 1{\cdot}33$ A. From the radius of I^-, $r(I^-) = 2{\cdot}16$ A., we may find its volume. We find for the volumes of ClO_4^- and I^- the values 3·94 and $4{\cdot}23 \times 10^{-23}$ cm.^{3} respectively. The experimental value[6] for the ionic volume of ClO_4^- is $4{\cdot}05 \times 10^{-23}$ cm.^{3}.

In order to check the hypothetical correlation between ionic size and its effect on the thyroid function, three ions which are isoelectronic with and of almost the same size as ClO_4^- were chosen. The similarity between perchlorate, monofluorosulphonate, difluorophosphate and fluoroborate ions has been pointed out[6,7]. The similarity of the ionic sizes of these ions may be deduced from the values of the bond-lengths in ClO_4^- (r(Cl—O) = 1·50 A.)[6], in sulphate (r(S—O) = 1·50 A.)[6], in phosphate (r(P—O) = 1·50 A.)[6] and in fluoroborate (r(B—F) = 1·48 A.)[8], and, on the other hand, from the fact that[5] $r(O^=) = r(F^-)$. In our experiments we compared, under identical conditions, the effects of the three ions mentioned above with that of perchlorate on the accumulation of iodine in the thyroid.

Monofluorosulphonate and difluorophosphate were synthesized by the reaction of ammonium fluoride with sulphur trioxide and phosphorus pentoxide respectively[9]; they were separated and purified by precipitation of their corresponding nitron complexes and finally their ammonium salts were recrystallized. Potassium fluoroborate was prepared from commercial fluoroboric acid and was recrystallized before use.

0·1 ml. of a 1 per cent solution of propylthiouracyl was injected into young rats (100–110 gm.) intraperitoneally, in order to block the formation of protein-bound iodine in the gland[3]. 1 hr. after this injection, 0·1 ml. of carrier-free iodine-131 iodide solution (40 mc./ml.) was injected. 15 min. later an injection of 0·5 ml. saline containing 25 μmoles of $KClO_4$, NH_4SO_3F, $NH_4PO_2F_2$ and KBF_4 respectively was given. The control rats were injected with 0·5 ml. of pure saline. The rats were killed at intervals of 30, 60, 90 and 120 min. after the iodide injection. The whole thyroid gland was removed and 1 ml. fresh blood was measured volumetrically and taken as a reference. The activity of the thyroid glands and of the blood samples was determined in a well-type sodium iodide scintillation counter. A summary of our experimental results is presented in Tables 1 and 2.

From the experimental results it is evident that all four ions tested are effective at these low concentrations. The increase in uptake with time of the $PO_2F_2^-$ series is most probably due to the hydrolysis of this ion[9] to F^- and $PO_4H^=$, which are not effective as inhibitors of iodide uptake[1]. It should be noted that these thyroid blocking agents have an effect within 15 min. after injection.

Other substances which accumulate in the thyroid, and thus interfere with its normal function, have been described lately, namely, TcO_4^- and ReO_4^-. Their accumulation in the thyroid was attributed to their position in the Periodic Table[10]. Evaluating the ionic volumes of these ions, we find[6] that the values for MnO_4^- and ReO_4^- are 4·0 and $4{\cdot}1 \times 10^{-23}$ cm.^{3} respectively; we may therefore infer that the ionic volume of TcO_4^- is $4{\cdot}05 \times 10^{-23}$ cm.^{3}, which actually is the experimental value found for the ionic volume of ClO_4^-. Thus we may include TcO_4^- and ReO_4^- in our series of effective monovalent anions.

It is worth while pointing out a correlation between the uptake of certain anions by the thyroid proteins and the fact that these very ions form insoluble complexes with nitron (1,4-diphenyl-3,5-endanilo-

Table 1. Activity of the Thyroid Glands (Counts/Min./Whole Thyroid)

Time (min.)	30	60	90	120
Control	78,670	129,270	83,840	71,350
$KClO_4$	8,420	8,630	10,150	6,740
NH_4SO_3F	33,500	8,200	23,050	22,440
$NH_4PO_2F_2$	20,630	7,220	17,850	58,670
KBF_4	8,480	8,200	6,250	9,620

Table 2. Relative Activity of the Thyroid Glands (Whole thyroid activity/activity of 1 ml. blood*)

Time (min.)	30	60	90	120
Control	1·80	4·45	3·20	2·90
$KClO_4$	0·15	0·13	0·26	0·34
NH_4SO_3F	0·70	0·38	1·00	1·09
$NH_4PO_2F_2$	0·45	0·24	0·66	2·16
KBF_4	0·11	0·11	0·14	0·29

* Taking the average weight of a rat's thyroid as 12 mgm. we may calculate the relative specific activity of the thyroid by multiplying the relative activity of the whole thyroid given in Table 2 by 833

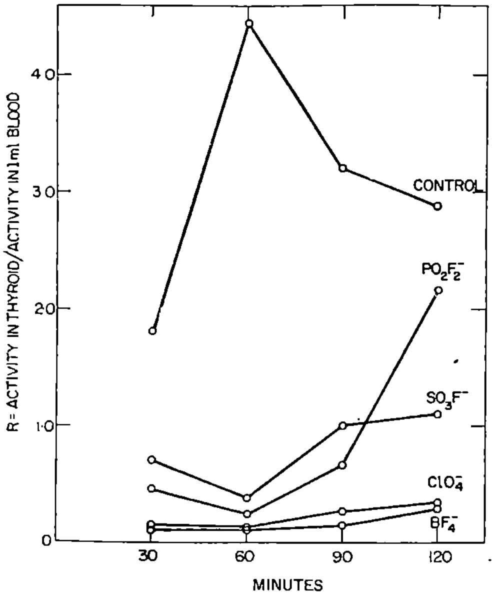

Fig. 1. Relative activity of thyroid glands of rats injected with inorganic blocking agents

4,5-dihydro-1,2,4-triazole). These ions include not only perchlorate and its isoelectronic species but also iodide, thiocyanate, chlorate and nitrate; all of them were found to take part in the function of thyroid[1]. The striking fact is that whereas chlorate has some effect on iodide uptake, no such effect was found for bromate[1]; it has been shown that iodate does not accumulate in the thyroid[11]. It has been shown[12], moreover, that nitron does not form insoluble complexes of appreciable stability with iodate and bromate.

It may be concluded that the trapping mechanism in the thyroid involves a factor which scarcely distinguishes between different anions having the same charge and a comparable volume. Such a factor is probably a protein with a special arrangement which traps only those ions which fulfil these requirements.

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In Vitro Effects of Insulin and Glucose on Leucine-2-^{14}C Incorporation into Protein of Diaphragms of Hypophysectomized Rats

INSULIN, added *in vitro*, has been found to stimulate the incorporation of labelled amino-acids into the protein of isolated diaphragms of normal rats[1-4]. Glucose, when added to the incubation medium, depressed the stimulatory action of insulin on the uptake of alanine labelled with carbon-14 [1,3] and α-amino*iso*butyric acid-^{14}C [4] by normal diaphragm. Even when insulin was not added to the incubation medium the uptake of these amino-acids was markedly depressed by supplementing the medium with glucose. In one report, however, the incorporation of glycine labelled with carbon-14 into protein of diaphragms of normal fasting rats was found to be increased by the addition of glucose alone to the medium[2]. A later study[3] failed to confirm this observation and indicated further that neither glucose nor pyruvate seriously altered the uptake of a number of amino-acids labelled with carbon-14 by normal diaphragm. From the above studies it was apparent that insulin had a stimulatory effect on the uptake of amino-acids by isolated muscle of normal rats, and that in certain instances this effect was altered by the concomitant utilization of carbohydrate. Thus, it was of interest to study the effects of insulin and of glucose, alone and in combination, on the *in vitro* incorporation of labelled leucine by the diaphragm of hypophysectomized rats, which show a decreased rate of incorporation of amino-acid[5] but which utilize glucose at a greater than normal rate[6].

Female rats (60 gm.) that were hypophysectomized three weeks previously were killed by a blow on the neck, and the diaphragm was quickly excised with part of the rib cage and spine attached and placed in freshly gassed buffer. The diaphragm was then divided into two hemi-diaphragms by cutting through the central ligament and through the insertions to the xiphoid process and spine. Each hemidiaphragm with ribs attached was blotted and placed in a 50-ml. Erlenmeyer flask and incubated with shaking for 90 min. at 37° C. The incubation flasks contained 6 ml. Krebs–Ringer phosphate buffer, *p*H 7·4, to which DL-leucine-2-^{14}C was added at a concentration of 0·1 m*M* (25,000 c.p.m./ml. medium). Each flask was gassed with 100 per cent oxygen during the first 2 min. of incubation and then sealed. Insulin (Lilly, crystalline, No. *T*-2842) was added to the medium at a concentration of 0·5 U./ml. and glucose was added at a concentration of 2 mgm./ml. medium. The incorporation reaction was terminated by rapidly chilling the flasks to 0° C. The tissue was then spread on a block of ice and the diaphragm muscle carefully trimmed of ribs and adhering tissue. The protein of the diaphragm was prepared and counted by methods published elsewhere[5].

The results are presented in Table 1. Insulin, added *in vitro*, increased the incorporation of leucine-2-^{14}C into the protein of diaphragms of hypophysectomized rats. Glucose added alone to the medium did not alter the incorporation of leucine by the diaphragms. Another experiment (not given in Table 1) with glucose added alone was carried out over a range of incubation times of 30–150 min., and again glucose addition had no effect on incorporation of leucine. When glucose and insulin were added together to the medium, the incorporation of leucine by the protein of the diaphragms was increased, but

Table 1. *In vitro* Effect of Insulin and Glucose on Incorporation of Leucine-2-^{14}C into Protein of Hypophysectomized Rats

Added to medium	No. of observations	c.p.m./mgm. protein	
		Mean	*S.E.*
Control	6	189	± 12·6
Insulin	6	287*	± 12·1
Glucose	6	186	± 22·4
Insulin + Glucose	6	280*	± 16·3

* Mean is significantly different from control, $P < 0{\cdot}01$.

the increment was similar to that produced by insulin alone (Table 1).

These results indicate that insulin *in vitro* stimulated the incorporation of labelled leucine into the protein of diaphragms of hypophysectomized rats. The addition of glucose to the medium, in the presence or absence of added insulin, had no effect on this system. These results agree qualitatively with those obtained in experiments with normal rat diaphragms[3]; but the increase in leucine incorporation produced by insulin in the hypophysectomized rat diaphragm (151 per cent of control) was greater than that reported for diaphragms of normal rats (118 per cent of control). The lack of an effect of glucose on this system would favour the opinion expressed by Manchester and Young[3] that the action of insulin in stimulating amino-acid incorporation is largely independent of its action on carbohydrate metabolism.

It is of interest that, like insulin, chronic bovine growth-hormone treatment begun seven days post-operatively resulted in a stimulation of *in vitro* leucine incorporation by diaphragms of hypophysectomized rats[5]. It is possible that this stimulation of amino-acid incorporation produced after growth-hormone treatment was due in part to an elevated insulin activity in the isolated diaphragm resulting from an increased secretion of insulin brought on by growth-hormone treatment. This seems unlikely, however, since bioassays of plasma insulin activity have failed to detect an increase in insulin activity when growth-hormone treatment was given to hypophysectomized rats 7–9 days post-operatively[7]. Moreover, growth hormone injected into hypophysectomized rats 18–24 hr. before removal of the diaphragm lowers the insulin activity bound to this tissue, as assayed by glucose uptake[8].

This study was conducted during the tenure of a National Research Fellowship in the Medical Sciences and was supported by a grant from the American Cancer Society (*P* 139-*A*) made to Dr. E. Knobil. I wish to thank Dr. Knobil for helpful criticism and Dr. Mary Root of Eli Lilly and Co. for generously supplying the crystalline insulin.

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Effect of Norleucine and Related Compounds on Growth of the White Rat

It was recently reported from this laboratory that the inclusion of 2 per cent DL-norleucine in the diet greatly inhibited the utilization of D-leucine by rats[1]. In view of this observation it was of considerable interest to determine whether the antagonistic effect of norleucine on leucine utilization was limited to the D-isomer of the latter.

The experiments summarized in Table 1 were designed to compare the effect of leucine isomers on the reversal of norleucine toxicity. Weanling albino rats of the Yale strain which were previously fed on a nitrogen-free diet for a 2-week period were used in this study. Following this period the animals were fed an amino-acid diet containing various levels of L- and D-leucine in the conjunction of 2 per cent DL-norleucine, as outlined in Table 1. The composition of the basal diet and the amino-acid mixture have been described elsewhere[2]. It can be seen from Table 1 that both enantiomorphs of leucine are antagonized by norleucine, but it is also apparent from the results that the antagonism is greater in the case of D-leucine. Although the exact quantitative relationship was not determined, it appears that at least twice as much of D-leucine is required to reverse norleucine toxicity when compared with the L-isomer. This is in good agreement with the previous observation that L-leucine is approximately twice as effective as the D-leucine for growth of young rats[2]. Note the close correlation between water consumption and growth.

Although norleucine does not seem to be a natural constituent of proteins[3] it is readily metabolized by mammals[4–7]. When incubated with rat liver homogenate it gives rise to α-ketocaproic acid, valeric acid and β-hydroxyvaleric acid. On the basis of such results, Kinnory *et al.*[8] concluded that norleucine is catabolized by conversion to the corresponding α-keto-acid, followed by oxidative decarboxylation and the subsequent oxidation to the resulting monocarboxylic acid by β-oxidation.

In order to learn more about the growth-depressing effect of norleucine an additional study was undertaken in which two of the above-mentioned intermediates of norleucine catabolism (α-ketocaproic and valeric acids) and two other compounds closely related to norleucine (caproic and ε-aminocaproic acids) were compared with norleucine for their effect on growth of rats. Since the growth-retarding effect of norleucine was previously demonstrated with the diet containing L-leucine at a level corresponding to 50 per cent of the requirement, that is, 0·43 per cent of the diet, it was decided to use this amount of L-leucine in our control diet. The compounds under test were added to the diet at molar equivalent levels corresponding to 1 per cent of norleucine. Normal weanling male albino rats of the Sprague–Dawley strain were used for assaying the above compounds. Each experiment covered 2 weeks. The experimental results which are shown in Table 2 demonstrate that of all the substances tested only norleucine and α-ketocaproic acid retarded the growth of rats. The slower rate of growth of animals was accompanied by lower consumption of food and decreased food efficiency. The inhibitory effect of the keto-acid is not unexpected since the first major step in the catabolism of most amino-acids, that is, formation of keto-acid, is readily reversible[9]. Since the keto-acid was less inhibitory than norleucine, while valeric acid

Table 1. AVERAGE GROWTH RESPONSE OF FOUR PROTEIN-DEPLETED WEANLING RATS TO L- AND D-LEUCINE IN THE PRESENCE OF DL-NORLEUCINE

Supplement to leucine-free diet	Days	Initial weight (gm.)	Final weight (gm.)	Change in weight (gm./day)	Water intake (ml./day)
0·85 per cent D-leucine + 2·0 per cent DL-norleucine	12	40	39	−0·08	5·6
1·70 per cent D-leucine + 2·0 per cent DL-norleucine	5	39	44	0·95	7·8
0·85 per cent D-leucine + 2·0 per cent DL-norleucine	6	44	42	−0·30	6·3
2·20 per cent D-leucine + 2·0 per cent DL-norleucine	4	42	50	1·90	9·2
0·43 per cent L-leucine + 2·0 per cent DL-norleucine	7	50	51	0·15	8·7
0·43 per cent L-leucine	3	51	62	3·55	12·3
0·43 per cent L-leucine + 2·0 per cent DL-norleucine	6	62	58	−0·60	10·5
0·85 per cent L-leucine + 2·0 per cent DL-norleucine	3	58	69	3·65	14·3
0·43 per cent L-leucine + 2·0 per cent DL-norleucine	9	69	67	−0·20	10·7

Table 2. EFFECT OF NORLEUCINE AND RELATED COMPOUNDS ON THE GROWTH OF WEANLING RATS FED DIETS LOW IN LEUCINE

Supplement to leucine-free diet	No. of rats	Initial weight (gm.)	Average weight gain (*W*) (gm.)	Average food intake (*F*) (gm.)	*W*/*F*
0·43 per cent L-leucine	4	57	16·0	71·5	0·22
0·43 per cent L-leucine + 1·0 per cent DL-norleucine	4	57	5·3	57·5	0·09
0·43 per cent L-leucine + 2·0 per cent DL-norleucine	4	57	2·0	62·0	0·03
0·43 per cent L-leucine + 0·99 per cent α-ketocaproic acid	4	57	8·5	56·0	0·15
0·43 per cent L-leucine + 0·78 per cent valeric acid	4	57	16·0	61·5	0·26
0·43 per cent L-leucine + 0·89 per cent caproic acid	4	57	19·3	73·5	0·26
0·43 per cent L-leucine + 1·00 per cent ε-aminocaproic acid	4	57	15·3	69·0	0·22

was without any demonstrable effect, it can be concluded that the deleterious effect manifested by norleucine is due to the intact molecule of the latter rather than to some of its catabolic products. Once the amino-acid undergoes oxidative decarboxylation it loses its growth-depressing effect. Since neither caproic nor ε-aminocaproic acids affected the growth of animals it is apparent that the amino- or oxo-group must be present at the α-carbon position in order to produce a growth depression in rats.

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Formation of Urea from Arginine in the Brain of the Living Rat

IN a classical set of experiments, Bollman, Mann and Magath[1] demonstrated that "the production of urea in the body of the dog is entirely dependent on the presence of the liver, since urea formation ceases completely as soon as the liver is removed". Standard text-books of physiology and biochemistry have interpreted the above experiments as demonstrating that urea formation occurs exclusively in the liver. However, an alternative interpretation is possible, namely, that normal liver function is necessary for normal extra-hepatic metabolism, and such extra-hepatic metabolism may include urea synthesis. In fact, it has been shown that perfused brain requires factors elaborated or released by the liver to maintain normal metabolism[2].

Recently, our laboratory has demonstrated that the brain of the rat can metabolize proline to ornithine and arginine *in vivo*[3]. Because of the role of ornithine and arginine in the Krebs urea cycle[4], it was of interest to determine whether brain is capable of metabolizing arginine to urea. The present report describes such experiments.

In studying metabolism of the brain of the intact animal it is essential to control the variable of extra-cerebral metabolism if one wishes to draw valid conclusions about cerebral pathways. In order to control the variables (1) extra-cerebral metabolism and (2) alterations in the metabolism of the brain and in the permeability of the blood-brain barrier resulting from an intracisternal injection, the rats used in these experiments were injected as follows: rats 2 and 4 were injected intracisternally with 1·2 mgm. of uniformly labelled ^{14}C-L-arginine monohydrochloride (total activity 37 μc.); 5 min. after their intracisternal injections these same rats were injected in the exposed femoral vein with 1·2 mgm. of inert L-arginine monohydrochloride. Rats 1 and 3 (litter mates, respectively, of rats 2 and 4) were injected intracisternally with 1·2 mgm. of inert L-arginine monohydrochloride, and 5 min. later were injected in the exposed femoral vein with 1·2 mgm. of uniformly labelled ^{14}C-L-arginine monohydrochloride (total activity 37 μc.). If, by the use of the above method, one can show that rats 2 and 4, which received radioactive arginine intracisternally, have more radioactivity in urea isolated quantitatively from brain than rats 1 and 3, which received the same dose of radioactive arginine intravenously, then one may conclude that the brain itself has the ability to metabolize arginine to urea.

All injections were performed under light ether anæsthesia, and all rats were alert and walking within a few minutes after injections were finished. The animals were killed by decapitation 1 hr. after their injection of radioarginine, and their brains homogenized in trichloracetic acid. Following the addition of 8 mgm. of inert carrier urea, the homogenates were centrifuged and urea was isolated from

Table 1. RADIOACTIVITY IN BRAIN 1 HR. FOLLOWING INJECTION OF RADIOACTIVE ARGININE. ALL ACTIVITIES EXPRESSED AS COUNTS PER MIN.

	Rat 1	Rat 2	Rat 3	Rat 4
Brain (wet weight, gm.)	1·680	1·750	1·750	1·760
Total activity of injected arginine	27×10^6	27×10^6	27×10^6	27×10^6
Total activity of brain trichloracetic acid-soluble fraction	$2\cdot9\times10^4$	810×10^4	$4\cdot2\times10^4$	810×10^4
Activity/mgm. of dixanthydryl urea isolated from brain	43	1,500	46	1,710
Total activity in brain urea	2,600	89,000	2,700	101,000

the fractions soluble in trichloracetic acid by chromatography on 'Dowex 50' columns. Complete separation of urea from other components soluble in trichloracetic acid was achieved by making the dixanthydryl derivative of urea, which was then recrystallized to constant specific activity.

The results presented in Table 1 show that dixanthydryl urea isolated from rats 2 and 4 is 35–37 times more radioactive than that isolated from their litter-mate controls, rats 1 and 3. The results thus indicate that brain can form urea from arginine. Since it has previously been demonstrated that rat brain can synthesize arginine from proline[3], it appears that brain is capable of urea synthesis *in vivo*. However, the quantitative significance of this pathway as a method of ammonia detoxication in brain is not yet known, and the role of urea synthesis in the metabolism of the brain remains to be determined.

We wish to express our appreciation to Dr. John Romano and Dr. George L. Engel for their support and encouragement during these experiments. Miss Ailene Williams contributed valuable technical assistance. This work was supported by grant *M*–1901 from the National Institute of Mental Health, U.S. Public Health Service and by the Foundations' Fund for Research in Psychiatry. A more detailed report of these investigations will appear elsewhere[5].

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Seasonal Variations in the Pituitary Gland of the Ferret

IT has been shown that the pars distalis of the pituitary gland of the cat, rabbit[1] and dog[2,3] contains cells which stain with carmine or acid fuchsin. These cells have been described as a second type of acidophile. They appear during the first pro-œstrous period in the young female cat, extend to occupy larger areas during œstrus and then partially regress[4].

Examination of the pituitary glands of female ferrets has shown that a similar type of carmine or fuchsin-staining cell is present, in addition to ordinary acidophiles which stain with orange *G* alone. After staining by the periodic acid – Schiff – orange *G* method[5] these 'carmine' cells appear deep reddish-orange in colour, in contrast to the yellow-orange of the acidophiles. This colour difference is due to a faint periodic acid – Schiff-positive reaction in the cytoplasm of the 'carmine' cells, combined with an affinity for orange *G*.

Pituitary glands of female ferrets killed at varying times of the year, and hence at varying phases of the breeding cycle, showed variations in the size and number of these cells. They were most numerous and widely distributed throughout the pars distalis in the glands of animals killed during early œstrus, and in four others which were anœstrous when killed in February, but which had been exposed to 16-hr. illumination each day for the three weeks before death. Bissonnette[6] showed that anœstrous ferrets reach full œstrus 38–64 days after exposure to extra light, and these four animals can almost certainly be considered to have been in an early pro-œstrous phase. In late œstrus, or early anœstrus, the cells were less conspicuous and reduced both in size and number; while in animals killed several months after the end of œstrus (November–January) the cells were either completely lacking or present only in small scattered groups. Vacuolation of the cells was seen in some, but not all, animals killed between August and December.

In the period immediately before œstrus, the cells are the largest of the various types in the pars distalis, and a Golgi zone similar to that found in basophiles is present in some of them. It seems probable that the increased size and number of these cells in the pro-œstrous period indicates that they are most active at this time; and this further suggests that they may be concerned with the initiation of œstrus.

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Measurements of Oxygen Tension in the Tissues of Mice cooled to 1° C.

Evans, Goodrich and Slaughter[1] demonstrated a decrease in the sensitivity to X-irradiation of the skin of new-born rats at body temperatures of about 0° C. Increased resistance to doses of X-rays which were lethal at normal body-temperatures has been demonstrated[2–3] at about 1° C. Weiss[4] has shown that there is increased resistance to radiation in the testes of mice subjected to whole-body X-irradiation at body-temperatures in the region of 1° C. It has been suggested by all of these authors that profound hypothermia acts by virtue of the anoxia which follows respiratory and cardiac arrest, and it is known that anoxia reduces sensitivity to X-irradiation[5].

We have recently attempted to measure oxygen tensions in the organs of mice while cooling, when

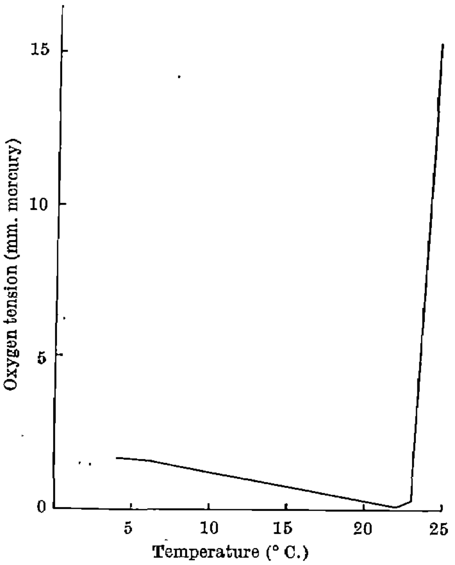

Fig. 1. Oxygen tensions recorded in the testis of a mouse resuscitated from 4° C.

cold, and also during resuscitation from the hypothermic state by the method of Goldsveig and Smith[6]. Gold electrodes (0·315 mm. diameter) insulated with 'Araldite' were inserted into spleen, testis and bone marrow and held in position by a stitch. A negative potential was applied (0·6 V. compared with a silver/silver chloride electrode inserted subcutaneously) and the resulting current was measured. Details of this oxygen–cathode technique for making quantitative measurements of oxygen tension will be described elsewhere (Cater, D. B., Silver, I. A., and Wilson, G. M., unpublished work).

Mice were cooled in sealed 1-lb. 'Kilner' jars immersed in ice, for 50 min. They were then removed from the jars, wetted with a detergent and surrounded by chipped ice, until their body temperatures measured per rectum fell to 0–1° C. After insertion of the electrodes, the ice was removed, the animals were warmed with a 60-W. electric light bulb, and given artificial respiration with a hand-pump.

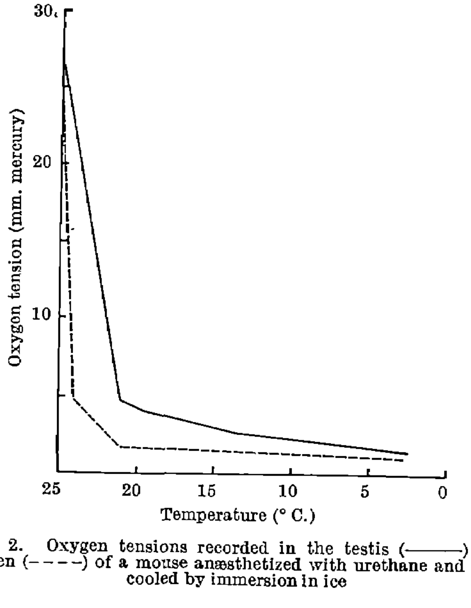

Fig. 2. Oxygen tensions recorded in the testis (———) and spleen (– – – –) of a mouse anæsthetized with urethane and then cooled by immersion in ice

The oxygen tensions recorded in the testis of a mouse, resuscitated from 4° C., are shown in Fig. 1. This experiment was discontinued when the animal showed signs of recovering consciousness.

It was not technically possible to make recordings of the oxygen tension in the organs of animals while they were being cooled down in a jar. However, mice were anæsthetized with subcutaneous injections of 25 per cent urethane in saline (0·25 ml./25-gm. mouse), and after the insertion of electrodes were cooled down in ice to 0–1° C. The recordings from the testis and spleen of such an animal are shown in Fig. 2. Respiration stopped in this mouse at 12° C.

The results showed that during cooling to the region of 0° C., the oxygen tension within the testis, spleen, bone-marrow and peritoneum fell reversibly to the order of 2 mm. mercury. This degree of hypoxia would be expected to afford considerable protection against radiation. The animals are protected from the effects of the hypoxia itself by their profound hypothermia. The possible applications of this to the radiotherapy of tumours will be discussed by one of us (L. W.) elsewhere.

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Target Organ Activation by Stress

It is a well-established fact that under stress conditions the organism calls for increased corticosteroid activity[1]. The response to such a call has been believed to occur solely by an increased corticosteroid production, that is, by increased pituitary-adrenocortical activity. Recent studies[2,3] have brought to light certain facts which suggest that the organism possesses an additional mechanism to meet the increased demand for corticosteroid activity. This mechanism functions by increasing the sensitivity of the target organs to corticosteroids.

The possibility of such a mechanism emerged during a study of the action of topically applied corticosteroids upon skin capillaries. It was noted that capillary resistance, measured by the negative pressure method, may increase under the local influence of corticosteroids in what appeared at first a haphazard manner. Further observation indicated that this increase in the response of the capillaries to corticosteroids is, in fact, a stress phenomenon.

An ointment containing 0·5 per cent Δ^2-hydrocortisone was applied on a circumscribed skin area of the flexor surface of the arm in human subjects or on the abdomen of dogs. The ointment base only was applied in the same manner on an adjacent control area. Five hours later the resistance of the

Table 1. Effect of Heavy Muscular Work (Gardening) on Capillary Resistance and Capillary Sensitivity of a 51-year-old Healthy Female Volunteer

A, Experimental day. Tests were applied at 7 a.m. (first line) and 2 p.m. (second line). Muscular exercise (arrow) was performed on the seventh day of experiment between the two testings. *B*, Capillary resistance (cm. mercury) in the skin area treated with cortisone. *C*, Capillary resistance in the control area. *D*, increase (+) or decrease (−) of the capillary resistance in cm. mercury in the cortisone-treated area as compared with the control area. An increase of more than 2 cm. was regarded as an indication of increased capillary sensitivity, that is, of capillary activation

A	*B*	*C*	*D*
5	11	12	− 1
	10	10	0
6	13	13	0
	12	11	+ 1
7	→ 13	12	+ 1
	24	16	+ 8
8	19	14	+ 5
	14	14	0
9	12	11	+ 1
	10	10	0
10	11	12	− 1
	12	10	+ 1

capillaries was measured in both areas (the value of capillary resistance is the least negative pressure expressed in cm. mercury which can produce one or more petechiae by rupturing the capillaries of the skin area tested). It was found that so long as the experimental subjects (two healthy volunteers and eight dogs) were leading a routine life and avoiding any extra stressful activity there was no difference between the resistance of the capillaries of the cortisone-treated and control skin areas amounting to more than ± 2 cm. mercury, the error of the method. The situation was markedly changed when stress was applied.

The human subjects did exhausting muscular work (swimming or gardening) or were exposed to ultra-violet light. On one subject the effect of delivering a strenuous class lecture was also studied. Dogs either ran in the treadmill or were irradiated by ultra-violet light or subjected to prolonged fasting. Following these various forms of stress the capillary resistance in skin area treated with cortisone was found to be significantly higher than in the control area in seven out of eight experiments in the human, and in eleven out of fourteen in the dogs. The differences showed wide individual variations amounting to 4–19 cm. mercury and were found to occur either within a few hours after stress or on the following day, and in most instances were demonstrable for several days. Two experiments, one in a human and one in a dog, exemplify in abbreviated form the phenomenon observed (Tables 1 and 2).

Table 2. Effect of a 25-day Fast (indicated between arrows) on Capillary Resistance and Capillary Sensitivity of an 18 kgm. Female Dog

For explanation see Table 1. Tests were made once daily between 1 and 2 p.m. During the period between the thirty-fifth and the forty-first days of the experiment no difference could be measured because capillary resistance in both areas was above the highest value measurable by the method (70 cm. mercury)

A	*B*	*C*	*D*
6	19	18	+ 1
8	19	20	− 1
10	19	19	0
12	20	18	+ 2
→ 14	21	20	+ 1
17	21	20	+ 1
19	24	19	+ 5
21	20	20	0
23	31	21	+ 10
25	27	20	+ 7
27	28	23	+ 5
29	30	25	+ 5
31	34	26	+ 8
33	30	30	0
35	> 70	> 70	
37	> 70	> 70	
→ 39	> 70	> 70	
41	> 70	> 70	
43	50	50	0
45	16	17	− 1
47	17	17	0
49	15	15	0

An attempt was then made to elucidate the mechanism by which capillaries are activated. There was no evidence that humoral factors play a part in this mechanism. Experiments on bilaterally sympathectomized dogs failed to demonstrate any capillary activation following stress. Activation was readily demonstrable in unilaterally sympathectomized dogs on the intact side but was entirely absent on the operated side. It appears, therefore, that activation, that is, increase in the sensitivity of the capillaries to corticosteroids, is intimately connected with the nervous system, specifically with the sympathetic nervous supply of the vessels.

The question whether or not other corticoid targets are activated by stress in a similar manner is open and does not appear to be as easily answerable as in the case of the capillaries. The present studies have in any event brought to light, through the specific example of the capillaries, a hitherto unknown ability of the organism to meet the demand induced by stress for increased corticosteroid activity in a manner other than by increased corticosteroid production.

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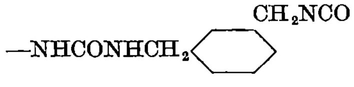
Preparation of an Electron-dense Antibody Conjugate

The fluorescent antibody conjugate technique recently developed by Coons[1] has already proved of great value in the study of biological problems. In this technique, a fluorescent substance is covalently linked to an antibody, and the antibody conjugate is allowed to react with cells or tissue containing its homologous antigen. The antigen is then detected and localized by observing the fluorescence in an optical microscope. For many reasons, it is desirable to extend this method to the sub-cellular level with the resolution attainable in the electron microscope. In order to achieve this purpose, however, it is necessary to confer sufficient electron density upon an antibody molecule, without inactivating it, to render it visible in the electron microscope.

We have prepared an electron-dense antibody conjugate by covalently coupling ferritin to the antibody. Ferritin is a crystalline protein of molecular weight 460,000 which is unique in that it contains as much as 23 per cent iron in ferric hydroxide–phosphate micelles[2]. Because of this electron density, individual ferritin molecules may readily be seen in the electron microscope[3]; they exhibit a characteristic micellar arrangement at the corners of a roughly square lattice.

The coupling of ferritin to the antibody was carried out as follows. To 5 ml. of a 1·6 per cent solution of crystalline horse spleen ferritin[2] in sodium borate buffer, *p*H 9·5, Γ/2 0·1 at 0° C., was added 0·10 ml. of *m*-xylylene di*iso*cyanate (the generous gift of the Carwin Co., North Haven, Connecticut). After ¾ hr. stirring at 0° C., the mixture was centrifuged, the supernatant solution was removed from the unreacted di*iso*cyanate, and was allowed to stand at 0° C. for an additional hour to allow any dissolved di*iso*cyanate to react. At this point, roughly half the free amino-groups of ferritin had reacted, presumably converted to



$$\text{—NHCONHCH}_2\text{—C}_6\text{H}_4\text{—CH}_2\text{NCO}$$

groups. This solution was then added to 5 ml. of a 1·6 per cent solution of rabbit γ-globulin (containing specific antibody), in the above-mentioned borate buffer containing, in addition, 1 *M* sodium chloride. After two days stirring at 6° C., the mixture was dialysed against 0·1 *M* ammonium carbonate to destroy any unreacted *iso*cyanate groups, and then was dialysed against phosphate buffer, *p*H 7·5, Γ/2 0·1. A small amount of precipitated protein was removed by centrifugation to give a clear stable solution.

To demonstrate that (*a*) the ferritin was conjugated to antibody, and (*b*) the ferritin–antibody conjugate was still capable of reacting specifically with its homologous antigen, the following experiments were performed. Two preparations of rabbit γ-globulin were available, one containing about 25 per cent anti-bovine serum albumin (BSA)Ab, the other about 20 per cent anti-bovine ribonuclease (RNase)Ab. Ferritin was treated with both by the procedure described above, giving preparations designated Fer-anti-BSA and Fer-anti-RNase, respectively. Two mixtures were then made, containing: (1) 2 mgm./ml. of Fer-anti-BSA and 1·5 mgm./ml. of unreacted anti-RNase γ-globulin; and (2) 3 mgm./ml. of Fer-anti-RNase and 1 mgm./ml. of unreacted anti-BSA γ-globulin, each in phosphate buffer, *p*H 7·5, Γ/2 0·1. 2-ml. portions of each mixture were then added to various dilutions of either RNase or BSA, and the precipitates formed after 24 hr. at 4° C. were washed and analysed for iron by the *o*-phenanthroline procedure, and for nitrogen by Nessler analysis.

Consider the results in the three upper sections (*A*, *B* and *C*) of Table 1. These clearly demonstrate that the presence of Fer-anti-BSA had no effect on the precipitation of RNase by anti-RNase, and therefore that the iron brought down in the RNase-(Fer-anti-RNase) precipitate must have been bound to specifically active antibody. Consistent with this conclusion is the essential independence of the iron/nitrogen ratio from the antigen/antibody ratio in the RNase-(Fer-anti-RNase) precipitates. Furthermore, if we assume that each Fer–Ab conjugate contains one ferritin and one antibody molecule, it follows from the iron/nitrogen ratios of 2·0 in our ferritin sample itself, and of 0·8 in the RNase-(Fer-anti-RNase) precipitates, that at least one-third of the antibody molecules were conjugated to ferritin. A larger fraction of antibody molecules could probably be coupled by using a larger mole ratio of ferritin to γ-globulin in the coupling reaction.

Table 1. FERRITIN–ANTIBODY COUPLING EXPERIMENTS

	Antigen (mgm.)	Antibody-containing γ-globulin	Antigen–antibody precipitates		
			N (mgm.)	Fe (mgm.)	Fe/N
A	RNase, 0·125	anti-RNase	0·044	0	0
	0·063		0·100	0	0
	0·031		0·083	0	0
	0·016		0·046	0	0
B	RNase, 0·125	{ anti-RNase Fer-anti-BSA }	0·039	0·008	0·21
	0·063		0·097	0·009	0·09
	0·031		0·090	0·008	0·09
	0·016		0·051	0·007	0·14
C	RNase, 0·125	{ anti-BSA Fer-anti-RNase }	0·009	0·015	—
	0·063		0·043	0·048	1·1
	0·031		0·149	0·119	0·80
	0·016		0·084	0·068	0·81
	0·008		0·049	0·046	0·94
D	BSA, 0·250	anti-BSA	0·058	0	0
	0·125		0·113	0	0
	0·063		0·089	0	0
	0·031		0·046	0	0
E	BSA, 0·250	{ anti-BSA Fer-anti-RNase }	0·008	0·003	—
	0·125		0·134	0·034	0·25
	0·063		0·125	0·064	0·51
	0·031		0·095	0·064	0·67
	0·016		0·061	0·057	0·93
F	BSA, 0·250	{ anti-RNase Fer-anti-BSA }	0·009	0·005	—
	0·125		0·067	0·049	0·73
	0·063		0·133	0·098	0·74
	0·031		0·078	0·052	0·67

In BSA-anti-BSA precipitations from solutions containing Fer-anti-RNase (section *E*, Table 1), some ferritin was brought down non-specifically. However, the iron/nitrogen ratio varied markedly with the antigen/antibody ratio in the precipitate. In particular, the iron/nitrogen ratio near the antigen–antibody equivalence zone was considerably smaller than the ratio in the specific BSA-(Fer-anti-BSA) precipitate (section *F*, Table 1). These results, therefore, while somewhat obscured by the non-specific precipitation, are consistent with the conclusions derived from the ribonuclease system.

The question of the specificity with which a Fer–Ab conjugate reacts with its homologous antigen is vital to the use of such conjugates in electron microscopic studies of cell and tissue sections. This question can only be answered at the electron microscopic level, however, and not by macroscopic antigen–antibody precipitation experiments. The specific behaviour of the RNase system, and the non-specific complications in the BSA system, are therefore not directly pertinent to this question.

Preliminary electron microscopic studies, in collaboration with Prof. William R. Adams, have indicated that in preparations of Fer–Ab conjugates, the characteristic micellar structure observed with ferritin itself is unaffected. These and further studies in progress, dealing with the application of the Fer–Ab conjugates to problems at the electron microscopic level, will be reported in detail elsewhere.

I gratefully acknowledge valuable discussions with Drs. Frank A. Pepe and Martin Saunders, and the competent technical assistance of Miss Julia McNeely.

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Inhibition of Electron Transport and the Swelling of Isolated Mitochondria

THE swelling of isolated rat-liver mitochondria appears under certain conditions to be dependent on their respiration[1]. This view is based on the following observations. (*a*) Mitochondria 'aged' by storage for one day in 0·44 *M* sucrose at 0° C. did not swell in presence of phosphate or thyroxine unless an oxidizable substrate was added as well. (*b*) With succinate as the substrate, malonate inhibited the swelling and amytal did not; whereas with β-hydroxybutyrate, amytal inhibited and malonate did not. (Amytal prevents oxidation of substrates with diphosphopyridine nucleotide-linked dehydrogenases, but has no effect on that of succinate[2].) (*c*) Cyanide inhibited swelling induced by phosphate, but not when electron transport was restored by addition of ferricyanide as terminal acceptor[3]. (*d*) Antimycin *A* inhibited swelling in presence of phosphate with various substrates[1,3]. The effects of amytal and antimycin on swelling have now been investigated further.

The experimental conditions have been described previously[1]. Antimycin in concentrations known to inhibit many mitochondrial oxidations[4] (3–50 mμgm./ml.) had only a small effect on the swelling induced by 10 m*M* phosphate or 30 μ*M* L-thyroxine with fresh mitochondria. In contrast, with aged mitochondria in the presence of 1 m*M* D-β-hydroxybutyrate, 5–8 mμgm. antimycin/ml. completely arrested the swelling induced by phosphate or thyroxine. However, when the β-hydroxybutyrate was replaced by L-glutamate, L-malate, L-proline or succinate (all 1 m*M*) the inhibition of phosphate-induced swelling was much less, and was only partial even with 50 mμgm./ml. (Fig. 1). A selective effect was observed with amytal as well. Unlike antimycin, amytal[2] (1·8 m*M*) completely arrested the swelling of fresh mitochondria induced by phosphate or thyroxine. With aged mitochondria, however, amytal resembled antimycin (Fig. 1), in that when β-hydroxybutyrate was present, a given inhibition was produced by a lower concentration of the barbiturate than that which was required with glutamate (Fig. 2).

Fresh mitochondria have been shown to contain substrates, for example, citrate[5] and precursors of glutamate[6], and to have a significant endogenous respiration[7]. It is therefore reasonable to suppose that the swelling of fresh particles is supported by oxidation of intrinsic material. We have seen that antimycin in the concentrations tested had little effect on the swelling of fresh mitochondria in absence of added substrate, whereas it was profoundly inhibitory with aged particles in presence of β-hydroxybutyrate. If this substrate were added to fresh mitochondria, it might be expected that antimycin would remain ineffective, swelling still being supported by the endogenous respiration, which is not sensitive to antimycin. Surprisingly, however, 5–50 mμgm. of antimycin/ml. strongly inhibited the phosphate-induced swelling of fresh mitochondria in the presence of β-hydroxybutyrate (Fig. 3). This suppression of the phosphate swelling was not obtained when β-hydroxybutyrate was replaced by malate; glutamate gave a slight effect. With ferricyanide present as terminal electron acceptor, antimycin had a similar action, that is, the phosphate-induced swelling, which was little affected by the antibiotic, was almost completely inhibited in the presence of β-hydroxybutyrate[3].

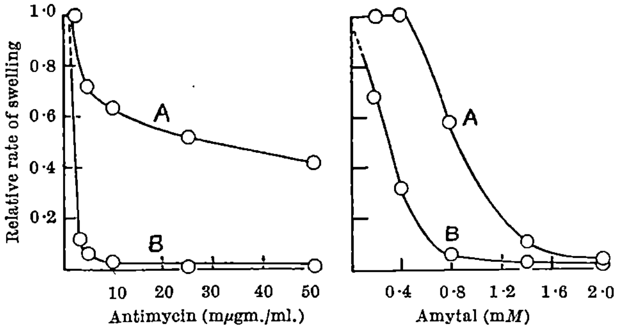

Fig. 1 Fig. 2

Figs. 1 and 2. Effects of antimycin *A* (Fig. 1) or amytal (Fig. 2) on the swelling induced by phosphate of aged mitochondria with 1 m*M* D-β-hydroxybutyrate or L-glutamate as substrates. The ordinates represent the steady rate of swelling in the presence of inhibitor relative to the maximal rate in an uninhibited control. Each cell contained 0·3 *M* sucrose, 25 m*M* *tris* chloride buffer, *p*H 7·5, and 10 m*M* phosphate. 20° C. Curve *A*, L-glutamate; curve *B*, β-hydroxybutyrate

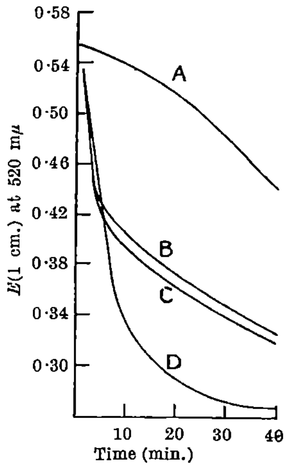

Fig. 3. Effects of antimycin *A* (20 mμgm./ml.) on swelling induced by phosphate of fresh mitochondria with and without D-β-hydroxybutyrate. Experimental conditions as for Figs. 1 and 2. Curve *A*, phosphate, β-hydroxybutyrate + antimycin; curve *B*, phosphate + antimycin; curve *C*, phosphate; curve *D*, phosphate + β-hydroxybutyrate

The action of the combination of β-hydroxybutyrate and antimycin was not restricted to fresh mitochondria, for with aged particles in which swelling due to phosphate was supported by glutamate, the further addition of DL-β-hydroxybutyrate together with antimycin completely checked the increase in volume, whereas antimycin alone caused an inhibition of only about 50 per cent.

In some respects oligomycin, which inhibits the phosphorylation system and thereby considerably reduces respiration in coupled systems[8], has an action on mitochondrial swelling like that of antimycin. Oligomycin (0·4 μgm./ml.) had a very small effect on the phosphate-induced swelling of fresh mitochondria, but when DL-β-hydroxybutyrate was present as well, almost complete inhibition resulted. In contrast to that of antimycin, this effect was counteracted by 2 : 4-dinitrophenol[3].

To summarize, it has been shown that antimycin and amytal caused an inhibition of mitochondrial swelling which depended on the substrate present; maximal sensitivity to these agents was observed when β-hydroxybutyrate was present, and minimal effects with no added substrate, that is, when the mitochondria were presumably dependent on their endogenous respiration. Other substrates showed behaviour between these extremes.

The protective action of β-hydroxybutyrate with fresh mitochondria in presence of antimycin or oligomycin is not readily explained in the light of our present knowledge. It seems to indicate an inhibition of endogenous respiration by β-hydroxybutyrate even when the oxidation of the latter is suppressed. Experiments are in progress, both with the oxygen electrode and with a new method for measuring ferricyanide reduction[3], to determine whether interaction of this kind takes place. If none is found, an explanation of our findings must be sought in terms of the respiration – swelling transducer mechanism.

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Methanol-soluble Carbohydrate Complexes

We have found that carbohydrates of low molecular weight are generally highly soluble in concentrated solutions of anhydrous calcium chloride in cold absolute methanol. After some time, crystalline methanol-solvated complexes of calcium chloride and carbohydrate are deposited. Such solutions and methanol-solvated complexes have not been reported before.

Lactose is the carbohydrate we have studied most thoroughly. A highly concentrated solution is prepared, for example, by mixing at 40° C. lactose, calcium chloride and methanol in a molar ratio such as 1 : 3 : 24. Paper chromatographic analysis of the aged solution shows that more than 97 per cent of the lactose remains unchanged and that a minor constituent has formed to the extent of less than 3 per cent. The specific rotations have been measured in water ; $[\alpha]_i$ refers to the value extrapolated to the instant of mixing with water, and $[\alpha]_f$ to the later equilibrium value ; the rotational effects of the calcium chloride and methanol are negligible under the conditions of measurement. That the α-form of lactose exists in higher proportion in methanolic calcium chloride solution than in water is shown by the ratio of $[\alpha]_i$ to $[\alpha]_f$, which equals 1·30. However, since $[\alpha]_f$ of the lactose in the methanolic solution is 43·5, while $[\alpha]_f$ of the lactose used as starting material is 55·3, the minor constituent which was found in the chromatographic analysis must have a very low or negative rotation.

From the highly concentrated methanolic solution, heavy crystallization occurs after months, or, when it is seeded and shaken, after several days or weeks. The crystals are separated by prolonged centrifugal filtration in a closed system, since they cannot be washed without change in composition. The crystals are first dried at 60° C. to evaporate the methanol, and then at 105° C. If heated first at 105° C., they decompose. Analysis shows that the crystals consist of 1 mole of lactose, 1 mole of calcium chloride, and 4 moles of methanol. Polarimetry shows that nearly all the lactose is present in its β-form.

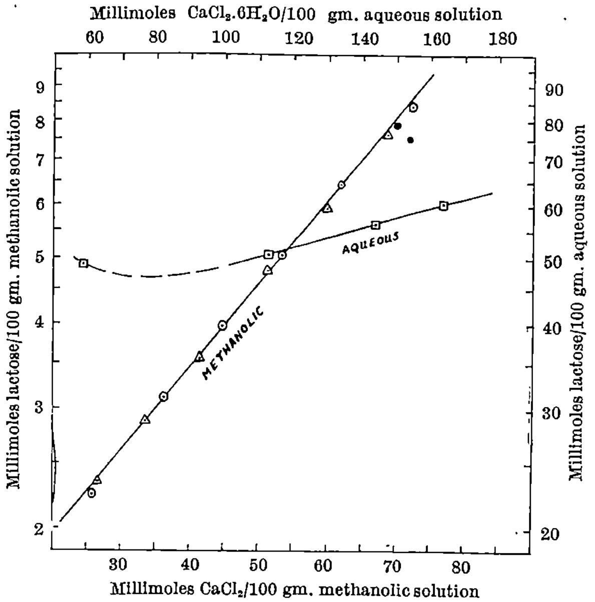

Fig. 1. △, ⊙, Solubility of lactose in methanolic calcium chloride, from two similar sets of experiments ; ⊡, solubility of lactose in aqueous calcium chloride, according to Herrington (ref. 1).

The dilution of the concentrated lactose solution with methanol causes lactose to crystallize. The ratio of $[\alpha]_i$ to $[\alpha]_f$ for these crystals equals 1·28 ; the final rotation $[\alpha]_f$ is 54·7. While this ratio is the same as exists in solution, these crystals do not contain the minor constituent which affects the final rotation in solution. Within the range investigated, the logarithm of the solubility of this crystallized lactose in methanol is a linear function of the calcium chloride concentration (Fig. 1). Herrington[1] determined the solubilities of lactose in aqueous calcium chloride solutions. If one plots (Fig. 1) the results of his four tests in which lactose was the solid phase, the logarithm of the lactose concentration turns out to be another straight line for the highest of three points ; the lowest point is off the line.

When about 6 moles of water are added to the highly viscous methanolic lactose solution for each mole of dissolved calcium chloride, the maximum amount of a complex consisting of (lactose. $CaCl_2$. $7H_2O$) gradually crystallizes over a period of a few days. Adding either more water or less lowers the yield. The lactose in these crystals is the α-form. These crystals are identical with those deposited from water according to Herrington's procedure[1].

Solubilities of several carbohydrates were determined in a qualitative way by the mixing of the carbohydrate with calcium chloride and methanol in a molar ratio of 1 : 3 : 24 at 28°. In general, monoses, bioses and trioses, and their simple derivatives were found soluble ; only the higher polysaccharides (for example, dextrin) are insoluble. The following are soluble : the sugars D-glucose, D-galactose, L-sorbose, D-fructose, sucrose, maltose, melezitose and raffinose, and the sugar derivatives α-methyl-D-glucoside, D-gluconolactone, sorbitol, lactobionolactone, and lactositol.

Some of the monoses, for example, glucose and fructose, crystallize very rapidly as methanol-solvated calcium chloride complexes. The fructose solution is of special interest in that soon after it begins to crystallize it becomes a translucent homogeneous rigid gel which fills the entire volume of the solution.

Methanolic calcium chloride might serve as a solvent for sugar reactions and for fractionating sugar mixtures by extraction or crystallization.

A fuller report is to be published elsewhere.

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Effects of Vanadium upon Liver Coenzyme *A* in Rats

THE addition of vanadium to liver sections of normal animals can prevent the synthesis of cholesterol from both mevalonic acid and acetate[1]. Diets containing vanadyl sulphate do not, however, alter the cholesterol-levels in the serum or liver after being administered for six weeks to rabbits fed on high-cholesterol diets, though they considerably reduce the cholesterol concentration in the aorta and appreciably lower the capacity of the liver to synthesize cholesterol[1,2].

On these grounds, a study was carried out aimed at assessing the effects of vanadium upon the liver coenzyme *A*—for it is an established fact that the synthesis of cholesterol from acetate is promoted by the activation of acetate by coenzyme *A*.

The first experiments were devoted to investigating the effects of vanadium upon the serum and liver cholesterol contents in (1) normal rats, (2) rats that had been kept on a high-cholesterol diet and (3) rats that had been administered intravenous injections of 'Triton' *WR* 1339 (arylalchylic phenol polyether) a surface-active substance that can enhance the cholesterol-synthesizing capacity of the liver[3]. Other experiments were devoted to assessing the effects of vanadium upon the coenzyme *A* of the liver.

The test were performed on white rats of our breeding, average weight 90–120 gm., fed *ad libitum* for 7 days before the experiment on a standard diet (diet *A*) of 21 per cent casein, 7 per cent olive oil, 4 per cent salt mixture IV, 5 per cent vitaminized lactose and 63 per cent sugar.

The hyperlipæmia from 'Triton' *WR* 1339 was determined by injecting the surface-active substance intravenously. Vanadium, in the form of an aqueous solution of sodium metavanadate ($NaVO_3.H_2O$), was simultaneously administered by intraperitoneal injection. The animals were killed by decapitation 18 hr. after the injection, and their sera and livers were analysed for total cholesterol by the Sperry–Webb[4] and Abell[5] methods, respectively.

Table 1. EFFECTS OF VANADIUM UPON THE CHOLESTEROL CONTENTS IN THE LIVER AND SERUM OF RATS UNDER VARYING EXPERIMENTAL CONDITIONS (AVERAGE VALUES ± S.E.)

No. of animals	Diet	Triton (mgm./kgm.)	Vanadium	Total cholesterol (mgm./100 gm. or 100 ml.) Serum	Liver
10	*A*	—	—	71·4 ± 4·33	204·5 ± 9·78
12	*A*	—	5 mgm./kgm. i.p.*	67·6 ± 3·48	182·9 ± 7·06
12	*A*	200	—	264·9 ±12·04	1,083·8 ±38·75
13	*A*	200	5 mgm./kgm. i.p.	197·2 ±11·81	741·8 ±21·14
15	*B*	—		80·6 ± 5·27	725·3 ±24·33
15	*B*	—	0·01 per cent in diet	74·9 ± 6·10	640·5 ±19·84
15	*B*	—	0·05 per cent in diet	76·6 ± 6·32	597·4 ±15·45

* i.p., intraperitoneal.

Table 2. EFFECTS OF VANADIUM ON THE COENZYME *A* IN THE LIVER OF NORMAL RATS (AVERAGE VALUE ± S.E.)

No. of animals	Vanadium	Days of treatment	Coenzyme *A* U./gm. liver	U./100 mgm. protein
12	—	—	138·1 ±3·75	103·5 ±3·29
15	5 mgm./kgm. i.p.*	1	135·7 ±3·49	94·9 ±3·12
15	5 mgm./kgm. i.p.	6	101·4 ±2·64	81·1 ±2·40
15	10 mgm./kgm. i.p.	1	83·0 ±2·12	68·5 ±2·18
12	0·01 per cent in diet	7	124·5 ±3·60	98·3 ±2·78
12	0·01 per cent in diet	14	97·6 ±2·35	84·7 ±2·11
12	0·05 per cent in diet	7	91·2 ±2·07	76·0 ±2·42
12	0·05 per cent in diet	14	68·5 ±2·15	59·4 ±1·29

* i.p., intraperitoneal.

The results are shown in Table 1, together with those concerning the effects of vanadium upon the cholesterol content of the serum and liver of normal subjects. In the same table the results obtained by administering vanadium for 7 days with a diet *A* containing an extra 1 per cent cholesterol (diet *B*) are also tabulated.

The effects on the coenzyme contents of the liver of vanadium administration, either parenterally or incorporated in our diet *A*, are tabulated in Table 2. The coenzyme content was determined by the Kaplan and Lipmann method[6] on two-thirds of each liver, the remainder being used for protein determination by the Folin method as amended by Lowry[7].

From Table 1 it can be seen that no significant changes occur in the cholesterol-levels in the liver and serum of normal animals 18 hr. after the vanadium injection. Now, since the same vanadium dose appears to lower to a fair extent the cholesterol-levels in the animals treated with 'Triton' the assumption that the metal exerts its effect only when cholesterol synthesis has been abnormally enhanced appears to be justified.

In animals kept on a high-cholesterol diet, the amount of cholesterol in the liver is reduced, though only to a moderate extent, even when only 0·01 per cent vanadium is added to the food. (The effect remains more or less unchanged as the vanadium percentage is increased.)

The effect of vanadium injected intraperitoneally on the coenzyme *A* of the liver becomes evident 24 hr. after a single administration of 10 mgm./kgm., or 6 days after a 5 mgm./kgm. daily dose.

When administered in the diet at a concentration of 0·01 per cent over 7 days, the metal does not seem to exert any significant action, the effects becoming apparent after a 14-day treatment. At a concentration of 0·05 per cent in the diet, a reduction in the coenzyme *A* of the liver is observable after 7 days; after a 14-day treatment it becomes considerable and may be as much as 40 per cent less than normal.

Our investigations have not yet detected the mechanism of the inhibiting action of vanadium upon the coenzyme *A*. Other workers[8] have suggested that the metabolism of sulphurated amino-acids would be affected by vanadium. If so, considering the important role of the thiolic cell components in biosynthesis of the coenzyme, a shortage might be postulated of the sulphydryl groups, notably cysteine, that are needed for the formation of pantotheine.

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Separation of Mono-*n*-butyl Phosphate and Di-*n*-butyl Phosphate by means of Ion Exclusion

Many different methods have been applied by several authors to the separation of mono- and di-*n*-butyl phosphate. Kumler and Eiler[1], who were interested in obtaining pure samples for the determination of their dissociation constants, used fractional precipitation of barium salts. Extraction by organic solvents (*n*-amylic alcohol or dibutylic ether) was applied with a good yield by Stewart and Crandall[2]; di-*n*-butyl phosphate is preferentially extracted into the organic phase. With the aim of obtaining mono- and di-*n*-butyl phosphate labelled with phosphorus-32, after the isotopic transfer of phosphorus-32 from $H_3{}^{32}PO_4$ to the esters, the exchange resin 'Dowex 2 *X*–8', 100–200 mesh, chloride form, was used by Higgins and Baldwin[3] to separate the three components from each other. Thus the mixture at *p*H 9 was fixed at the top of the resin bed; *ortho*-phosphoric acid, mono- and di-*n*-butyl phosphate were consecutively obtained by eluting with 0·05 *M* hydrochloric acid and with 0·5 *M* potassium chloride.

Separations of the same type were also carried out in our laboratory with satisfactory results, by using 'Amberlite *IRA* 400', carbonate form, and 0·1 *M* sodium carbonate and 0·1 *M* sodium chloride as selective eluants.

To investigate another way of separation, some ion exclusion experiments were carried out by us. This method needs no regeneration of the resin, which acts with a different mechanism from that of common ionic exchange. Many factors are reported to determine the limitations of ion exclusion[4]; among them are: rate of flow of solution through the column; volume of feed and concentration ratio of the two components; operating temperature; size of resin particles and percentage of cross-linkage; degree of dissociation of compounds to be separated. In principle, separation through ion exclusion is effective when compounds involved possess different degrees of dissociation, because one component acts as an 'ionic substance' in respect to the other 'non-ionic'.

Even though mono- and di-*n*-butyl phosphate have nearly the same dissociation constants[1] (for mono-*n*-butyl phosphate $K' = 1{\cdot}29 \times 10^{-2}$, $K'' = 1{\cdot}40 \times 10^{-7}$ and for di-*n*-butyl phosphate $K = 1{\cdot}90 \times 10^{-2}$) a fairly good separation was obtained by operating in the conditions reported below. A bed of 50 c.c. of 'Dowex 50 *X*–8', 50–100 mesh, hydrogen form, having a cross-section of 1·1 cm.^{2}, was fed with 9 ml. of a solution containing 0·071 m.moles/ml. of mono-*n*-butyl phosphate and 0·037 m.moles/ml. of di-*n*-butyl phosphate at a flow-rate of 6·25 ml./hr. cm.^{2}. While eluting at room temperature (18° C.), with distilled water at the same rate of flow, fractions of 2·2 ml. were automatically collected. Results are shown in Fig. 1, where mono-*n*-butyl phosphate is shown appearing after 18 ml. of effluent and di-*n*-butyl phosphate after 38 ml., as was expected on a theoretical base. Furthermore, it should be pointed out that mono-*n*-butyl phosphate, in spite of its slightly lower dissociation constant, is eluted first. The yield of separation is 95·5 per cent in pure mono- and 89 per cent in pure di-*n*-butyl phosphate, since in one fraction alone the two components were both present. Rate of flow can be raised to 9 ml./hr. cm.^{2} and feed concentration varied at about ±10 per cent without influencing the separation yield, which is lowered only when the amount of resin is reduced by 20 per cent.

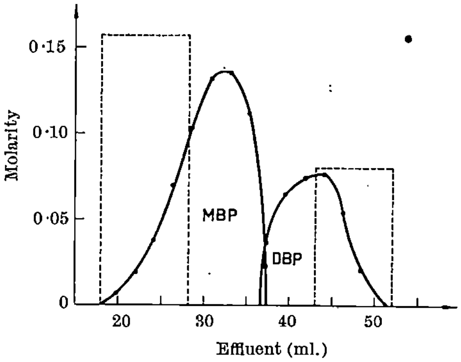

Fig. 1. Elution curves for mono- and di-*n*-butyl phosphate. Dashed lines indicate the theoretical shape of the separation

To prepare significant amounts of pure compounds, seven semi-continuous cycles were carried out, on 650 c.c. of resin, 5·2 cm.^{2} cross-section. Each cycle employed 100 ml. of feed solution containing 0·061 m.moles/ml. of mono-*n*-butyl phosphate and 0·028 m.moles/ml. of di-*n*-butyl phosphate, at a rate of flow of 9 ml./hr. cm.^{2}.

All the experiments described here were performed on solutions of mono- and di-*n*-butyl phosphate obtained synthetically from phosphorus pentoxide and butanol, and brought to suitable concentrations by dilution with water.

Analyses of fractions were carried out by potentiometric titration with 0·1 or 0·01 *N* sodium hydroxide; in some cases a purity control by paper chromatography was effected[5].

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Structure of Dihydrodiphosphopyridine Nucleotide

WEBER[1] has recently reported on the intramolecular transfer of excitation energy in dihydrodiphosphopyridine nucleotide. In addition to the strong band having its maximum at 340 mμ, the excitation spectrum of the 462 mμ fluorescence also shows a maximum at 260 mμ, a region where the absorption is due to the purine part of the molecule.

Kaplan *et al.*[2] have identified an isomer of diphosphopyridine nucleotide which comprises 10–15 per cent of a highly purified commercial preparation of diphosphopyridine nucleotide. The isomer was characterized by optical rotation studies as the α-glycoside of nicotinamide riboside as distinct from the biologically active β-isomer of diphosphopyridine nucleotide. This assignment of configuration about the C_1 of ribose was substantiated by the synthetic preparation of nicotinamide mononucleotide[3] to give a mixture of the β- and α-anomers in a 4 : 1 ratio.

The α-isomer of diphosphopyridine nucleotide was reduced chemically with sodium dithionite[4] and the product was examined spectrofluorometrically. Unlike the β-isomer, the excitation spectrum of the 462 mμ fluorescence of α-dihydrodiphosphopyridine nucleotide shows a strong band only when activated at 340 mμ and not when irradiated at 260 mμ, indicating that excitation energy transfer is not as efficient with the α-isomer as was observed with the β-isomer. The 462 mμ fluorescence resulting from 260 mμ and 340 mμ excitation of α- and β-dihydrodiphosphopyridine nucleotide is shown in Fig. 1.

Further evidence for the differences in interaction in the α- and β-isomers of dihydrodiphosphopyridine nucleotide may be found in their spectrophotometric behaviour in water and propylene glycol. Weber[1] reported that the ratio E_{260}/E_{340} is 2·85 for the intact β-isomer of dihydrophosphopyridine nucleotide, whereas this ratio becomes 3·4 in propylene glycol. A similar examination of the reduced α-isomer reveals that the E_{260}/E_{340} ratio is the same in water as in the propylene glycol.

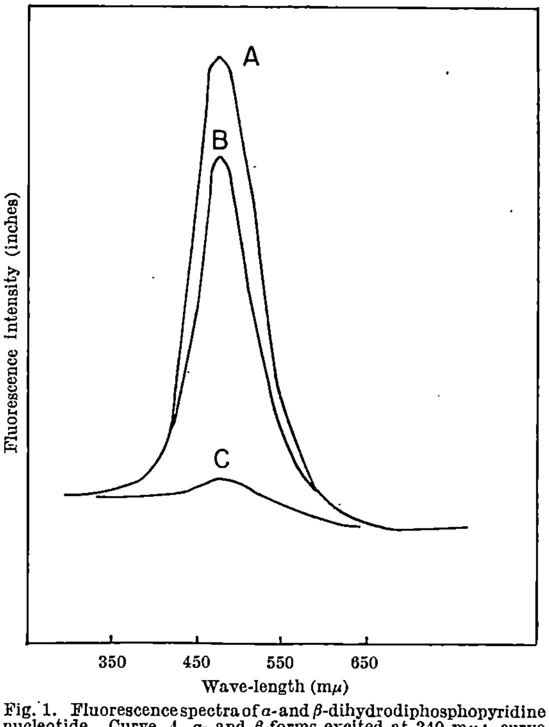

Fig. 1. Fluorescence spectra of α- and β-dihydrodiphosphopyridine nucleotide. Curve *A*, α- and β-forms excited at 340 mμ; curve *B*, β-form excited at 260 mμ; curve *C*, α-form excited at 260 mμ. These values are relative since the intensities of the exciting light have not been determined

Studies similar to those described for the α-isomer of dihydrodiphosphopyridine nucleotide have been carried out with deamino-dihydrodiphosphopyridine nucleotide (the hypoxanthine analogue[5]) and with the 3-acetylpyridine analogue[6]. The latter analogue clearly showed the transfer of excitation energy since excitation at 260 mμ gives a 478-mμ fluorescence[7] which is also elicited by excitation at 365 mμ. The absorption spectrum of this analogue behaved much like β-dihydrodiphosphopyridine nucleotide in water and propylene glycol. The deamino-dihydrodiphosphopyridine nucleotide, however, did not show properties of energy transfer, since excitation of the purine ring did not result in fluorescence of the dihydropyridine nucleus.

In accordance with the postulate by Weber[1] that the adenine and the dihydropyridine rings form a complex in β-dihydrodiphosphopyridine nucleotide, it appears that such complex formation cannot occur in the α-isomer.

Further studies on the structural conformation of diphosphopyridine nucleotide and dihydrodiphosphopyridine nucleotide are being examined in this laboratory through the use of pyridine coenzyme analogues.

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A Possible Negative Feedback Phenomenon controlling Formation of Alkaline Phosphomonoesterase in *Escherichia coli*

WE have already reported[1] that in a phosphate-deficient medium the amount of ribonucleic acid in *E. coli* decreased remarkably, while there was an appreciable increase of deoxyribonucleic acid, protein and viable cell numbers. At the same time we also studied activities of some enzymes presumed to be related to the degradation of ribonucleic acid, for example, ribonuclease phosphodiesterase and phosphomonoesterase, and found a marked increase in that of phosphomonoesterase. This communication is concerned with this formation of phosphomonoesterase in *E. coli*.

The strain used was *E. coli B* and the medium contained per litre: 3·0 gm. NaCl, 0·25 gm.

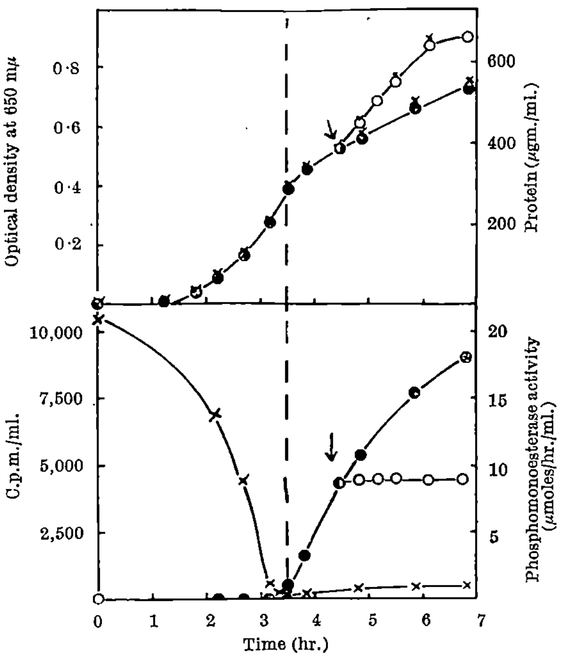

Fig. 1. Relation between the formation of phosphomonoesterase and phosphate content in the medium. Cells were suspended in a medium containing phosphorus-32 at 10 μgm. phosphorus/ml. and incubated at 37° C. with shaking. At the time indicated aliquot samples were taken to assay phosphomonoesterase activity and protein content (see text). At the time indicated by arrows, the culture was divided into two portions, to one of which (○—○) was added phosphate (100 μgm./ml.) and to the other (●—●) water. Radioactivity of the medium was obtained from that of the supernatant fraction after centrifugation (10,000*g*; 5 min.). The broken line indicates the time when the phosphate in the medium was exhausted. ●, ○, Optical density; ×, protein concentration

$MgSO_4.7H_2O$, 0·01 gm. $CaCl_2$, 2·0 gm. sodium lactate, 10·0 gm. Difco 'Bactopeptone' and 12 gm. *tris*-(hydroxymethyl)-aminomethane. The *p*H was 7·4. This medium contained 16 μgm. phosphorus/ml. Phosphomonoesterase activity was measured by the method of Bessey *et al.*[2], using *p*-nitrophenyl phosphate as the substrate, glycine–sodium hydroxide buffer (*p*H 9·5) and magnesium sulphate. Activity of phosphomonoesterase was expressed as μmoles of *p*-nitrophenyl phosphate hydrolysed/hr./ml. of toluene-lysed cell suspension[3]. Protein was estimated by the method of Lowry *et al.*[4] using bovine serum albumin as standard.

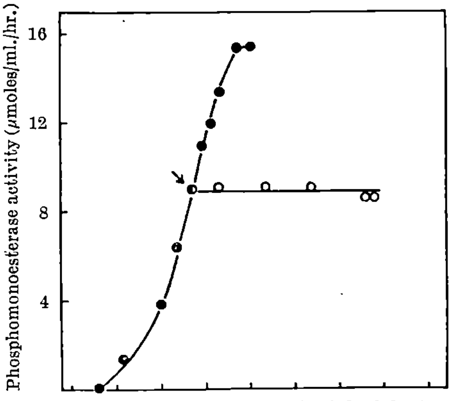

Fig. 2. Relation between the activity of phosphomonoesterase and optical density of the culture. Experimental conditions and key as in Fig. 1

As illustrated in Fig. 1, cells began to form phosphomonoesterase when the phosphate in the medium was exhausted. Thereafter, a linear increase of activity was observed for 2–3 hr. and the amount of cell protein/ml. increased linearly, although at a low rate. Fig. 2 shows the relation between the increase of optical density and that of the phosphomonoesterase activity. As shown in Fig. 2 this increment of protein was directly proportional to that of phosphomonoesterase activity, except in the early and in the final phases of the phosphate-deficient stage. The formation of phosphomonoesterase was stopped immediately by the addition of phosphate to the medium (final concentration: 100 μgm. phosphorus/ml.), though the amount of protein increased at a high rate (Figs. 1 and 2). The appearance of phosphomonoesterase activity was not observed in the phosphate-rich medium. Apparently phosphate inhibits the action of phosphomonoesterase.

In view of the above results, it seems to us that the formation of phosphomonoesterase is an important factor in the regulation system of the phosphate economy in *E. coli*. A negative feedback mechanism[5] is possible, with phosphate as a repressor, although the activation of phosphomonoesterase cannot be ruled out. Further details will be published elsewhere.

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RADIOBIOLOGY

Effect of High Oxygen Pressure on the Protective Action of Cystamine and 5-Hydroxytryptamine in Irradiated Rats

Both the oxidized disulphide, cystamine (—S—S—) and its corresponding sulphydryl amine, cysteamine (—SH) are excellent radioprotective agents *in vivo*[1]. If rats, protected by the latter reduced substance, respire pure oxygen under pressure (4–5 atmospheres absolute) at the time of irradiation, the protective action is completely reversed[2,3] and this result also applies to cysteine. Our own findings have shown that this reversal also applies to the pharmacologically active amines, histamine and adrenalin, and largely to 5-hydroxytryptamine (*vide infra*). The lessening of the radioprotective action of these reducing agents by an increased oxygen pressure in tissue fluids may be due to the inactivation of additional —SH and reducing groups supplied to the body, or due to an increase in physical solution and diffusion of oxygen so provided, in overcoming the anoxæmia caused by either decreased oxygen-carrying capacity of hæmoglobin (for example, with *para*-aminopropiophenone[3]), or by smooth muscle constric-

Table 1. Fffect of Respired Oxygen Pressure on the Protective Actions of Cystamine and 5-Hydroxytryptamine against Acute Radiation* Lethality in Rats† and Effect of Added Pretreatment with Sodium Cyanide

Experiment	Respired gas (pressure in atmospheres absolute)	Survivors at 30 days (per cent)	Mean survival over 30 days (± *S.D.*)
1	Air (1 atmosphere)	6/9 (67)	25·90 (± 6·80)
	Oxygen (2 atmospheres)	6/10 (60)	24·90 (± 8·31)
	Oxygen (4 atmospheres)	7/9 (78)	25·00 (± 9·59)
	Oxygen (5 atmospheres)	4/10 (40)	21·60 (± 10·84)
2	Air (1 atmosphere)	6/9 (67)	26·10 (± 7·00)
	Oxygen (2 atmospheres)	6/10 (60)	22·10 (± 10·38)
	Oxygen (4 atmospheres)	1/9 (11)	13·00 (± 9·11)
	Oxygen (5 atmospheres)	2/9 (22)	12·11 (± 10·43)
3	Air (1 atmosphere)	5/10 (50)	22·90 (± 9·18)
	Oxygen (2 atmospheres)	4/10 (40)	20·30 (± 9·37)
	Oxygen (4 atmospheres)	2/10 (20)	13·90 (± 9·00)
	Oxygen (5 atmospheres)	0/10 (0)	8·60 (± 1·24)
4	Air (1 atmosphere)	2/10 (20)	17·90 (± 8·36)
	Oxygen (2 atmospheres)	2/10 (20)	14·10 (± 10·30)
	Oxygen (4 atmospheres)	1/10 (10)	11·40 (± 7·72)
	Oxygen (5 atmospheres)	0/10 (0)	9·50 (± 3·15)

Experiment 1. Rats pretreated with cystamine‡ (15 mgm.).

Experiment 2. Rats pretreated with sodium cyanide§ (2 mgm.) and cystamine‡ (15 mgm.).

Experiment 3. Rats pretreated with 5-hydroxytryptamine‡ (2 mgm.)

Experiment 4. Rats pretreated with sodium cyanide§ (2 mgm.) and 5-hydroxytryptamine‡ (2 mgm.).

* All animals received 1,000 r. X-rays whole-body irradiation.

† Rats of Canberra black stock weighing 150–190 gm., of equal sexes.

‡ Cystamine or 5-hydroxytryptamine administered as intraperitoneal injection 5 min. preceding irradiation.

§ Sodium cyanide administered intraperitoneally 5 min. prior to injection of protective agent (cystamine or 5-hydroxytryptamine).

tion in bronchioles or arterioles resulting from pharmacological action (for example, 5-hydroxytryptamine[4]). However, the protective disulphide, cystamine (—S—S—), is reduced to cysteamine (—SH), *in vivo*[5] and *in vitro*[6], and increased oxygen pressure *in vivo* may be expected to lessen its protective action, if the latter depends on the reduction of cystamine in tissues, to produce available —SH groups, or promote pharmacological activity, both of which tend to result in intracellular anoxia.

Our studies of the effect of respired oxygen tension on the protective action of cystamine and 5-hydroxytryptamine in rats subjected to acute lethal whole-body irradiation show that an increase in respired oxygen pressure to 4 and 5 atmospheres absolute pressure almost completely reverses the protective action of 5-hydroxytryptamine but fails to cause significant reduction in the protective action of cystamine. An example of the experimental results is given in Table 1. It is seen that pretreatment with sodium cyanide, itself a reducing substance but not protective in rats[7,8], results in a substantial reduction in the protective action of cystamine (and 5-hydroxytryptamine) if combined with increased oxygen pressure. In other experiments in which the dose of cystamine was reduced to 4, 8 and 12 mgm./rat respectively, raised oxygen pressures (4 atmospheres absolute) also failed to decrease the lesser protective action resulting and, indeed, tended to enhance the protective action to levels corresponding to a higher dosage of cystamine.

The results indicate that the protective action of cystamine (—S—S—) does not result entirely from the formation *in vivo* of cysteamine (—SH), although the enhancement of protective action at lower dose levels may support the hypothesis of Pihl and Eldjarn[9] that the degree of protective action is correlated with the ability to form mixed disulphides. That protective action for the disulphide depends on its histamine-liberating qualities[10] is not supported by our findings with histamine protection and its reversal by oxygen respired at 2 atmospheres absolute[8]. Again, the effect of combined cyanide pretreatment and oxygen pressure (Table 1) fails to support the theory of free-radical competition as applied to radioprotection *in vivo* of either cystamine or reducing substances, and a decrease of intracellular oxygen pressures (delayed by pretreatment with respiratory enzyme poisons) seems to be at least an important contributing factor. If the transfer of oxygen across cellular membranes involves active transport mechanisms, as distinct from simple physical diffusion, it may be easier to interpret chemical protection in terms of an 'oxygen effect'. These studies will be reported in full elsewhere.

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Effect of X-Rays on the Cell

It is well known that the inhibition of the synthesis of nucleic acid plays a very important part in the chain of the post-irradiation changes and particularly in the blocking of mitosis. But this hypothesis does not explain the great susceptibility of mitosis to comparatively small doses of irradiation[1]. The generalization relating sensitivity to mitotic activity fails when applied to lymphocytes. Other important biochemical processes in the cell, as, for example, the oxidative phosphorylation, are also sensitive to irradiation[2]. It cannot be excluded that other cellular functions are also impaired by X-rays.

We were able to demonstrate that, as yet, unknown changes[3] occur in tissue after small doses of irradiation. We incubated the tissue homogenate at 38° C. and found that coagulation occurred in a homogenate prepared from the organ of the irradiated rat, whereas coagulation did not occur in a similar homogenate prepared from tissue from a non-irradiated animal. We found this effect with the spleen, and also with 'radioresistant' liver tissue.

The coagulation phenomena may best be followed with the aid of turbidometric measurements. The present communication reports some properties of liver homogenates from irradiated and non-irradiated rats, studied by this method and by *p*H measurements.

The animals generally used in our experiments were Wistar albino rats of both sexes. We used a 'Super Sanax' X-ray apparatus operated at 180 kV. and 15 m.amp. with 1-mm. aluminium and 0·5-mm. copper filters, focus distance 53 cm., dose-rate 40 r./min. Animals were killed by decapitation 30 min.

after irradiation. The liver was removed after perfusion *in situ* with cold physiological saline and gently homogenized in distilled water (1 gm. in 10 ml.). We used a chilled loose Potter–Elvehjem glass homogenizer (about 20 up-and-down strokes of the pestle, driven at 1,500 rev./min.). Colorimeter tubes were filled with the whole homogenate, consisting chiefly of disrupted and partly of whole cells (after filtration through mill cloth) and the increase of optical density during incubation was measured against water using a green-yellow filter. In some experiments we measured the *p*H of the homogenate during the incubation (ionoscope apparatus) with antimony and calomel electrodes at 22° C.

We found that the coagulation of the homogenate from irradiated rats takes place more quickly in comparison with the coagulation of the control. It is interesting that it is possible to prove by this method the effect of a dose of 10 r. The speed of coagulation depends on the dose of irradiation (Table 1).

Table 1

Irradiation dose	Time of incubation at 38° C. required to reduce light transmission of homogenate by 50 per cent (average for 3 rats)
500 r.	265 min.
100 r.	295 min.
10 r.	375 min.
Control	425 min.

Raising the temperature of incubation accelerates the coagulation of the liver homogenate from the irradiated animal as well as that of the control. The *p*H in liver homogenate from irradiated animals falls more rapidly than that from controls (Fig. 1).

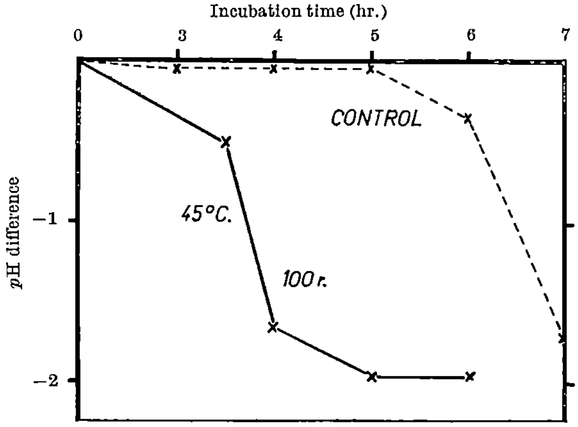

Fig 1. Drop in the *p*H of liver homogenate from irradiated and non-irradiated rats

We studied similar phenomena on spleen homogenate. It coagulates faster than liver homogenate, however, so that it is more difficult to demonstrate the influence of small doses of irradiation in that case.

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PATHOLOGY

Prevention of Adaptive Formation of Tryptophan Peroxidase by a Carcinogenic Azo Dye

The carcinogenic azodye 3′-methyl,4-dimethyl aminoazobenzene induces gross tumours in livers of rats fed a basal diet poor in riboflavin[1]. The whole process, in Sprague–Dawley rats, takes approximately 200 days. Structural damage to liver tissue may be detected histologically during the first weeks of carcinogen feeding[2]. Intracellular changes, manifested by the gradual depletion of mitochondria and ergastoplasm, which result in respiratory damage to the cell, can be detected by differential centrifugation weeks and even months before onset of malignancy[3]; yet all these changes are long-range effects. Even though the continual administration of this carcinogen brings about respiratory damage to the cell, the carcinogen is not a respiratory inhibitor[4,5]. It can be shown that the specific respiratory activity (activity per mgm. protein nitrogen) with sodium pyruvate as substrate remains normal for mitochondria during feeding with this carcinogen although the tissue is full of protein-bound azodye[5]. In short, the immediate chemical effect of this carcinogen, apart from its binding to one or more proteins not yet functionally characterized[6], is still obscure.

Assuming that the depletion of cytoplasmic structures may be due to the interference of the carcinogen with some phase of the mechanism of protein synthesis, we decided to study its effect on adaptive enzyme formation. It is known that tryptophan peroxidase is an adaptive enzyme formed in mammalian livers in increased amounts following the injection of L-tryptophan[7]. The enzyme is synthesized *de novo* by the liver cell from its constituent amino-acids[8]. It was reported recently[9] that there exists in the hepatoma a block in the pathway of tryptophan metabolism via kynurenin, indicating the absence of tryptophan peroxidase. There seem to be no results, however, in the literature on the level of this enzyme and its adaptive synthesis in the precancerous liver. For these reasons we investigated the induction of tryptophan peroxidase in livers of Sprague–Dawley rats (two months old at the beginning of the experiment) fed for various lengths of time on a basal diet containing 3′-methyl,4-dimethyl aminoazobenzene (twice recrystallized, 600 mgm./kgm. of food) as compared with controls on a basal diet without the carcinogen.

L-Tryptophan (78 mgm. in 10 ml.) was injected intraperitoneally to half the animals; the other half remained uninjected. 6 hr. after injection all animals were killed. The liver tissue was homogenized in isotonic neutral potassium chloride. Tryptophan peroxidase was assayed by the spectrophotometric method of Knox[10] from metaphosphoric acid extracts of samples incubated at 37° C. for 60 min. and unincubated controls. The sediments obtained after precipitation with 15 per cent metaphosphoric acid were extracted by Schneider's procedure[11] and the deoxyribonucleic acid was measured by the diphenylamine reaction. Assuming 5×10^{-12} gm. to be the constant deoxyribonucleic acid content of a rat diploid nucleus[12], the results expressed on this basis indicate the activity of tissue per nucleus.

Table 1 shows that there is no manifest change in tryptophan peroxidase activity in the course of 80 days of carcinogen feeding. On the other hand,

Table 1. Effect of Feeding 3′-methyl,4-dimethyl aminoazobenzene on Adaptive Synthesis of Tryptophan Peroxidase

Time (days)			0	10	25	30	35	80
Basal diet	Non-injected	Activity DNA Spec. act.	0·420 702 0·300	0·724 740 0·489	0·484 570 0·368	0·287 544 0·263	0·429 700 0·300	0·640 576 0·556
	Tryptophan-injected	Activity DNA Spec. act.	1·550 786 0·987	1·580 552 1·436	1·240 500 1·240	1·130 584 0·966	1·410 700 1·007	1·672 524 1·024
		Increase Percentage	0·687 229	0·947 195	0·882 240	0·703 168	0·707 230	1·024 184
Basal diet plus carcinogen	Non-injected	Activity DNA Spec. act.		0·620 750 0·413	0·384 530 0·359	0·366 764 0·476	0·420 500 0·420	0·440 760 0·290
	Tryptophan injected	Activity DNA Spec. act.		1·130 675 0·836	0·480 530 0·452	0·476 572 0·417	0·829 700 0·440	0·550 692 0·410
		Increase Percentage		0·423 100	0·093 25	0	0·020	0·120 40

Activity = μmoles of kynurenin formed in 1 ml. homogenate in 1 hr. at 37° C. DNA = μgm. in 1 ml. homogenate. Spec. act. = activity per 5×10^{-12} gm. DNA.

the ability to form new tryptophan peroxidase after the injection of tryptophan declines rapidly in 10 days, and is later either zero or very low compared with the controls. Fractionation of tissue homogenized in isotonic sucrose has shown that tryptophan peroxidase is present only in the soluble phase of the cell, remaining in the supernatant after the components of the broken ergastoplasm have been spun down by centrifugation for 1 hr. at 59,000*g* in the 'Spinco' preparative ultracentrifuge. Thus, feeding the carcinogen, rather than inhibiting tryptophan peroxidase, prevents the cell from forming new soluble protein.

In order to decide whether the drop in adaptive enzyme formation is due to structural damage or to a block of the enzyme-forming system we administered single massive doses of the carcinogen (40 mgm. in 10 ml. corn oil) intraperitoneally to rats kept on a basal diet for four weeks prior to the experiment. The controls were injected with corn oil alone. 17 hr. after intraperitoneal injection half the control animals and half the experimental animals (3 of each) were injected with tryptophan. A parallel test indicated that in animals treated with the carcinogen a large amount of the carcinogen was protein-bound and could be liberated only after prolonged hydrolysis of tissue[6]. Assay, performed 6 hr. after injection of tryptophan, showed a substantial inhibition of tryptophan peroxidase formation in rats which received carcinogen.

We believe that these results provide evidence that 3′-methyl,4-dimethyl aminoazobenzene blocks the synthesis of tryptophan peroxidase, and possibly of other soluble proteins, by the enzyme-forming system of the hepatic cell.

Table 2. Effect of a Single Injection of 3′-methyl,4-dimethyl aminoazobenzene on Adaptive Synthesis of Tryptophan Peroxide

Corn oil	Non-injected (3 animals)	Activity DNA Spec. act.	0·600 744 0·400
	Tryptophan injected (3 animals)	Activity DNA Spec. act.	1·300 608 1·060
		Increase Percentage	0·660 165
Corn oil plus carcinogen	Non-injected (3 animals)	Activity DNA Spec. act.	0·418 530 0·400
	Tryptophan injected (3 animals)	Activity DNA Spec. act.	0·612 604 0·505
		Increase Percentage	0·105 25

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Enterotoxicity of Bacteria-free Culture-filtrate of *Vibrio cholerae*

Two Ogawa strains of *V. cholerae* maintained for six months in the laboratory by fortnightly subculture on agar slopes, and two Inaba strains maintained similarly for about eighteen months have been used for this study. All the strains, which were smooth, were checked for their identity and particularly for their inability to lyse sheep red blood cells. 5 ml. of an 18-hr. culture of each strain in Dunham's peptone water medium was aseptically transferred to a 1-litre Roux bottle containing 200 ml. of a sterile medium of the following composition and a *p*H of 7·6: 'Bacto-peptone' (Difco), 5·0 gm.; sodium chloride, 0·5 gm.; water, 100 ml.

The bottle was laid flat in the incubator, with a maximum free surface of the medium exposed to the air, for about 18 hr. The liquid culture was spun in a 'Servall' superspeed centrifuge in the cold room (2–4° C.) for 10 min. to throw down the bulk of the bacteria. The supernatant was cleared further by high-speed centrifugation for 20 min. at about 14,000 r.p.m., at about 18° C. The clear supernatant fluid was filtered under suction through a Courtauld (later Oxoid) membrane filter. The filtrate was tested for sterility by inoculating 0·1 ml. into 2 ml. of each of Dunham's peptone water and of nutrient broth and incubating for about 42 hr. If unsterile, it was refiltered until sterile. 1 ml. of the sterile filtrate was injected slowly (taking 45–60 sec.) into the lumen of 4-in. loop of rabbit small intestine isolated by two silk ligatures. Essentially, a previous technique for studying the mechanism of action of *V. cholerae* on the intestinal mucous membrane was followed. A second loop of the same length in the same animal about one foot away from the first, was injected with the control medium (5 per cent peptone) treated in a similar way. Next morning, the animal was killed and changes in the loops were looked for. From the first preparation, three such experiments were performed. Two more preparations from the same (Ogawa) strain and three from each of the remaining three strains were tested once each on rabbit loops.

Each of the fourteen control loops was collapsed, and very little fluid, if any, could be expressed from inside them. All fourteen loops receiving culture filtrates were distended with fluid. Some appeared pale, in others blood vessels on the outer wall looked as if they had been injected, while still others appeared hæmorrhagic. The contained fluid was either like rice water, slightly pink, or definitely red. The volume of the contents was about 10 ml. and showed evidence of the presence of mucus, a few epithelial cells and a variable number of red blood corpuscles. The centrifuged supernatant was alkaline (pH 8–9) and had the following composition: nitrogen, 0·69 mgm./ml.; sodium, 144 m.equiv./l.; potassium, 5·6 m.equiv./l.; chloride, 85 m.equiv./l. Nitrogen was determined by Kjeldahl's method, the others by flame photometry. Cultures of scrapings from the mucous surface of the loops were negative to *V. cholerae*. The histological picture of the wall of the swollen loops was variable and included œdema of the mucosa and/or submucosa, infiltration of the mucous membrane with lymphocytes and occasional polymorphonuclear cells, congestion of the blood vessels and some denudation of surface epithelium. In places, the villi seemed to have disappeared altogether, leaving only a thin strip of mucous membrane still attached to the muscular wall. The control loops did not show any histological change.

Three filtrates prepared from an 18-hr. culture of an Ogawa strain in Dunham's peptone water medium, and one filtrate from each of the other three strains grown similarly did not produce any gross or microscopic change in the rabbit loops.

Further details of the activities of different filtrates will be published elsewhere. I am grateful to the Principal, Medical College, Calcutta, for permission to publish this work and to Dr. D. M. Bose, director, Bose Institute, for giving me full facilities of his laboratories. My thanks are due to Dr. Amitabha Sen for helpful criticisms, to Dr. M. L. Ghose for help in the animal experiments, and to Prof. M. L. Chakrabarty for carrying out the flame photometry.

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Influence of L-3′,5,3-Triiodothyronine on the Oxidative Phosphorylation of Tumour Mitochondria

THE tumour cell differs from the normal cell mainly in its strong unco-ordinated growth. As any form of growth is combined with an increased consumption of energy, the tumour cell must consequently possess an increased energy metabolism compared with that of the normal cell. This increased expenditure of energy of the malignant cell cannot be completely explained by substrate oxidation via the tricarboxylic acid cycle, as the respiration of the tumour cell is no greater than that of the normal cell. According to Warburg[1] the respiration of tumour cells is even less than that of corresponding normal cells. As is well known, glycolysis, that is, the reduction of carbohydrates to lactic acid, which takes place also under aerobic conditions, is considered as a source of the additional energy production.

The synthesis of energy-rich phosphate bonds, which is coupled with respiration, is decisive for the energy production of the cell, that is, the so-called oxidative phosphorylation. According to Martius[2], Lehninger[3] and other authors, oxidative phosphorylation can be uncoupled by several substances. In this way the synthesis of energy-rich phosphates is disturbed and the cell suffers from energy deficiency.

Similarly, with regard to the energy metabolism of the tumour cell, it should be possible to disturb its energy balance with uncoupling substances and thus to retard the growth. Now, the vitality of a cell which is disturbed in its energy metabolism is impaired and that cell is inferior compared with other normal cells. Therefore, tumour cell damaged in this way should more easily succumb to the body's defence mechanisms and should also be more effectively influenced by cytostatica or radiotherapy. Starting from this hypothesis, we tested triiodothyronine, which was discovered by Martius[4] and Lehninger[5] to be an uncoupling agent of oxidative phosphorylation. As already reported[6], in optimal concentration it reduces tumour growth. Now it seemed to be essential to prove that triiodothyronine uncouples oxidative phosphorylation of tumour mitochondria, too. This, at first, does not appear to be obvious as its uncoupling effect depends on a 'swelling effect' of the mitochondria[5], but the membrane of tumour mitochondria differs considerably in its permeability from the membranes of normal mitochondria[7] and accordingly an uncoupling effect is not necessarily to be expected.

Table 1 shows the influence of triiodothyronine on the oxidative phosphorylation of mitochondria from Walker carcinoma. The mitochondria were isolated from necrosis-free tumour slices in an isotonic sucrose solution and were employed without previous treatment by triiodothryonine.

The comparatively high phosphorus/oxygen ratios of the tumour mitochondria where triiodothyronine was not added results from their greatly reduced respiration. This is possibly a consequence of the impaired respiration of tumour cells postulated by Warburg[1].

We consider that the considerable increase of X-ray sensitivity in experimental tumours and human cancers after administration of triiodothyronine, as recently demonstrated by Stein and Griem[8], can, partially at least, also be explained by a disturbance in the fundamental processes of oxidative phosphorylation. In addition, our experi-

Table 1. INFLUENCE OF TRIIODOTHYRONINE ON OXIDATIVE PHOSPHORYLATION.

The medium contained: 100 m.moles potassium chloride, 35 m.moles magnesium chloride, 10^{-3} m.moles cytochrome *c*, 12 m.moles keto-glutaric acid as substrate, 21 m.moles potassium dihydrogen phosphate, 10 m.moles adenosine monophosphate, 40 m.moles glucose, 30 units hexokinase and 50 m.moles histidine and hydrochloric acid to neutralize it. Triiodothyronine $7 \cdot 5 \times 10^{-5}$ moles, *p*H 7·4. Each deposit contained also 0·5 mgm. or 2·0 mgm. diphosphopyridine nucleotide. The respiration of the mitochondria was measured according to the Warburg technique, temperature 28° C., duration of experiment 20 min. The phosphate was determined according to Fiske and Subbarow (ref. 8)

Triiodo-thyronine added	DPN added (mgm.)	O_2 uptake (μmoles)	P (μmoles)	P/O	Inhibition (per cent)
No	0·5	2·0	4·6	2·3	—
Yes	0·5	2·1	0·64	0·3	87
No	2·0	2·5	3·5	1·4	—
Yes	2·0	3·7	0·31	0·1	93

ments on various malignant neoplasms lead us to believe that the sensitivity of tumours to cytostatica is also considerably increased experimentally and clinically by combined treatment with uncoupling agents like triiodothyronine. A more detailed report of this work will be published later.

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A Cytopathogenic Agent from a Mammary Tumour in a *C3H* Mouse that produces Tumours in Swiss Mice and Hamsters

Stewart, Eddy *et al.*[1-3] recently reported that an agent derived from leukæmic *AK* mouse tissue produces a cytopathogenic effect in cultures of mouse embryo cells. Furthermore, after passage in tissue culture, this agent, which they term the S.E. Polyoma virus, produces a variety of tumours when it is injected into newborn Swiss mice and hamsters. This report describes observations on an agent with similar properties but derived from a different source.

Tissue from a mammary tumour in a *C3H*/Jax retired breeder was homogenized in a Potter–Elvehjem homogenizer and centrifuged at low speed. The supernatant was frozen. Later it was thawed, and 0·3 ml. added to a single Carrel flask culture of normal *C3Hf*/HeHa mouse kidney cells maintained in a medium consisting of *CMRL*-1066[4] supplemented with 20 per cent horse serum. An uninoculated sister culture was kept as control. The media were changed on the third and ninth days. A cytopathogenic effect was first observed in the inoculated culture on the twelfth day, and was extreme on the thirteenth day. The culture fluid was centrifuged gently, and 0·1 ml. of the supernatant was added to each of several cultures of mouse kidney cells. Cytopathogenic effects were then observed after 4 days. Ten further consecutive passages were made and at each passage a cytopathogenic effect was seen 3–6 days after the culture was inoculated.

The virus is cytopathogenic for normal kidney cells from two different sublines of *C3H* mice (*C3H*/StHa and *C3Hf*/HeHa), and for kidney cells and embryo cells of Swiss *ICR* mice. It has no apparent effect on kidney cells of monkey or rabbit. It remains cytopathogenic after being kept at − 10° C. for 3 months, or at 37° C. for 3 hr., or at 57° C. for 30 min. It has caused hæmagglutination of normal rabbit and guinea pig erythrocytes in titres to 1 : 2560.

Tissue culture fluid from the fifth passage was injected into 50 Swiss mice on the first or second day after birth. The mice exhibited early stunting and poor hair growth similar to that described in newborn mice injected with the polyoma virus[2]. 45 mice survived to weaning. Tumours were observed from the fourth month after injection. To date, nine months after injection, 16 mice have developed a total of 18 tumours. Eleven had parotid tumours, 3, all virgin females, had mammary adenocarcinomas, 2 had thymic lymphomas, and one had all three types.

53 newborn Swiss mice were injected with fluid from normal cultures of *C3Hf* kidney cells. Of these, 48 survived to weaning. No stunting was observed in these mice. Five months after injection, a parotid tumour was observed in one, and to date 3 have developed parotid tumours, and one had both a parotid tumour and a thymic lymphoma. The fact that these mice developed tumours suggests that they received some virus. There are at least three possible ways that this could have occurred: (1) the control cultures could have become contaminated with virus from the inoculated cultures; (2) tumour virus could have been present in the *C3H* tissues used to initiate the control cultures, and this would be consistent with the observation of Gross[5] that extracts of normal organs of *C3Hf* mice injected into newborn mice of the same strain can induce parotid tumours; or (3) the newborn mice might have become infected by air-borne virus. In considering these possibilities it should be mentioned that Mirand[6] has also observed tumours to develop in newborn mice injected with control culture material, and Buffett *et al.*[7] have shown that tumours sometimes develop in animals kept in close contact with others that were injected with subcellular particulates from tumours.

Ten of the tumours in our experimental group have been examined in the electron microscope. In two of these, large numbers of extracellular virus-like particles were observed (Fig. 1), and in four others, smaller numbers were seen. The particles were about 110 mμ in diameter, and many had a dense, central nucleoid body. No particles were seen in the remaining tumours. Three tumours that appeared in mice injected with fluid from normal cultures have been examined, and no particles have been found.

Virus from the twelfth passage was injected into newborn Syrian hamsters. A high percentage have already developed tumours, with deaths occurring from these tumours as early as ten days after injection.

Thus we have obtained, from a *C3H* mouse mammary tumour, a cytopathogenic virus with broad tumour-inducing properties. This may be a new tumour virus. But at least two other possibilities must be considered. First, our findings are so

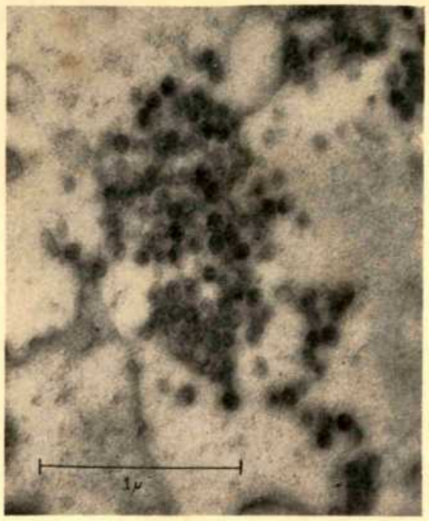

Fig. 1. Electron micrograph showing virus-like bodies in a parotid tumour induced in a Swiss mouse by the cytopathogenic tumour virus derived from *C3H* mouse mammary tumour

similar to those of Stewart and Eddy that they raise the question of whether or not we are dealing with the same virus as theirs. Since we were not carrying the polyoma virus in our laboratory at the time when the injections were made, our preparations could not have been contaminated with polyoma virus. The polyoma virus was obtained from leukæmic tissue of *AK* mice and ours was obtained from a *C3H* mouse mammary tumour. Therefore, if our virus is indeed the polyoma virus, it would mean that the *C3H* mammary tumour and the *AK* leukæmic tissue must have contained the same virus. There is no direct experimental evidence bearing on this point. Secondly, since the tumour from which our extract was made contained the milk agent[8,9] it is possible that this latter virus induced the variety of tumours which we observed. If so, we must assume that passage in tissue culture increased the pathogenicity of the virus to account for the wide tumour-inducing properties not hitherto associated with the milk agent. Finally, it is possible that our results could be accounted for by not one, but a mixture of viruses.

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MICROBIOLOGY

Production of Acid from Arabinose and Xylose by Strains of *Azotobacter*

During investigations on the utilization of pentoses by *Azotobacter*, production of acid was observed in many cases in media with arabinose or xylose as sole source of carbon. This acid production is easily demonstrated by inoculation of nitrogen-free agar plates containing 0·5 per cent xylose and 0·5 per cent glucose and undissolved calcium carbonate. In this medium a distinct clear zone develops around the colonies (Fig. 1).

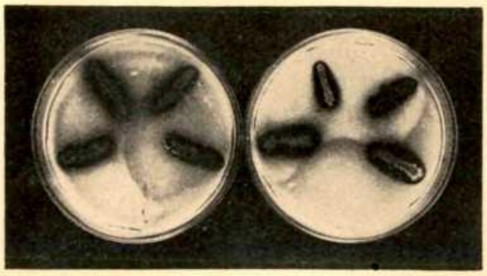

Fig. 1. Nitrogen-free agar plates with 0·5 per cent xylose and 0·5 per cent glucose and undissolved calcium carbonate, inoculated with 10 *Azotobacter* strains, of which eight show acid production

The *Azotobacter* strains were partly stock cultures kept from earlier investigations and partly new isolates from samples of garden soil. The basal medium used had the following composition (gm.): KH_2PO_4, 0·2; K_2HPO_4, 0·8; $MgSO_4 \cdot 7H_2O$, 0·2; NaCl, 0·2; $CaSO_4 \cdot 2H_2O$, 0·1; $Fe_2(SO_4)_3$, 0·01; $Na_2MoO_4 \cdot 2H_2O$, 0·005; 'Bacto' agar 1·0, in 1,000 ml. distilled water, *p*H 7·2. The pentoses were added in concentrations of 0·5 per cent.

*p*H determinations were made with a glass electrode after 14 days incubation at 25° C. The results are recorded in Table 1. Most of the cultures showed no visible growth. Only 5 strains of *A. chroococcum* and 1 strain of *A. beijerinckii* were able to grow well with arabinose as sole carbon source, and xylose was not utilized at all by these species. The strains of *A. vinelandii*, on the other hand, were better able to utilize both arabinose and xylose, although visible growth was in no case accompanied by acid production.

In subsequent experiments with 3 strains of *A. vinelandii*, production of acid, breakdown of xylose, and nitrogen fixation were measured simultaneously (Table 2). The acid produced was determined by back titration to the initial *p*H. Xylose was determined by the method of Somogyi, and nitrogen by the Kjeldahl method. The strains *P*-3 and *P*-4 showed

Table 1. *p*H Values of Cultures on Pentose Media after 14 Days Incubation at 25° C.

	Number of strains lowering *p*H to				
	4·0–4·4	4·5–4·9	5·0–5·4	5·5–5·9	6·0–7·1
Arabinose					
A. chrooc.	0	4	0	2	20
A. beij.	0	0	0	0	7
A. vinel.	0	0	0	0	10
Total	0	4	0	2	37
Xylose					
A. chrooc.	18	6	0	0	2
A. beij.	4	1	0	0	2
A. vinel.	5	0	0	1	4
Total	27	7	0	1	8

Table 2. DECOMPOSITION OF XYLOSE, FIXATION OF NITROGEN AND PRODUCTION OF ACID BY STRAINS OF *A. vinelandii* IN MEDIA WITH XYLOSE AS SOLE SOURCE OF CARBON. (INITIAL XYLOSE CONTENT ABOUT 100 MGM.)

Strain	Final *p*H	Acid produced (m.equiv.)	Nitrogen fixed (mgm.)	Xylose decomposed (mgm.)	Equivalent acid/ moles xylose	Mgm. nitrogen fixed/ gm. xylose decomposed
P-3						
Without	4·40	0·117	0	17	1·0	0
$CaCO_3$	4·37	0·117	0	17	1·0	0
With	—	—	0	92	—	0
$CaCO_3$	—	—	0	92	—	0
P-4						
Without	4·34	0·119	0	21	0·9	0
$CaCO_3$	4·38	0·121	0	23	0·8	0
With	—	—	0	87	—	0
$CaCO_3$	—	—	0	85	—	0
P-5						
Without	6·89	—	0·45	55	—	8·2
$CaCO_3$	6·90	—	0·45	56	—	8·0
With	—	—	0·47	56	—	8·4
$CaCO_3$	—	—	0·47	54	—	8·7

no visible growth and no nitrogen fixation could be detected, but distinct production of acid had taken place with simultaneous disappearance of xylose. In cultures without calcium carbonate this process was soon inhibited by the acid reaction, and only about one-fifth of the xylose was decomposed with production of about 1 equivalent of acid/mole of xylose. In cultures with calcium carbonate, however, four-fifths or more of the xylose was decomposed. Unlike these two strains, *P*-5 was able to utilize xylose and showed rather good growth. No production of acid had taken place and growth was equally good with or without calcium carbonate.

The decomposition of carbohydrates by *Azotobacter* is not normally accompanied by production of acid, but acid formation may take place in certain circumstances, and a few cases have been recorded previously[1]. Jensen proposes as a possible explanation that strains of *Azotobacter* can oxidize certain carbohydrates to the corresponding sugar acids, but are unable to metabolize these acids further, and this theory is supported by the ratio between acid production and carbohydrate dissimilation in the above experiments. The enzymes concerned with this initial oxidation are probably less specific than those concerned with the later steps of decomposition. No proof of these theories is available yet, but at least it seems clear that the breakdown of carbohydrates by *Azotobacter* follows a scheme different from that of Embden–Meyerhof, with production of acid in one of the initial reactions.

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The Phenylalanine Test on Kligler's Iron Agar for the Identification of *Proteus*

BUTTIAUX and his colleagues[1] have questioned the reliability of the urea test for the identification of members of the genus *Proteus* in routine investigations of Enterobacteriaceae. They found many urease-negative *Proteus* strains, and, using Stuart's urea medium[2] they, moreover, detected many urease-positive strains of the genus *Paracolobactrum*.

The Providencia group, now renamed *Proteus inconstans* in the latest edition of "Bergey's Manual of Determinative Bacteriology"[3], is generally urease-negative. All *Proteus* strains, however, are able to deaminate phenylalanine oxidatively to phenylpyruvic acid, a reaction which other members of the Enterobacteriaceae are unable to effect. Buttiaux and his fellow-workers consider the phenylalanine test, which demonstrates this deamination, to be a much more reliable characteristic of *Proteus* than the urea test. Henriksen's[4] method of performing the phenylalanine test, and that of Buttiaux and his colleagues, described in the paper cited above, are too complex and time-consuming for many laboratories. Ben Hamida and Le Minor[5] devised a simple and rapid test using harvested cells from an agar slope, shaken in a buffered solution of phenylalanine; phenylpyruvic acid being tested for, after 10 min. shaking on a Kahn shaker, by the addition of a ferric chloride solution. An intense green coloration was positive, for the presence of phenylpyruvic acid.

This technique seemed admirably suited to adaptation, preferably with the view of extending the use of another diagnostic medium such as Kligler's iron agar, the cells washed from such a culture serving as the suspension for the phenylalanine test.

Forty or so strains of various members of the Enterobacteriaceae, including 18 in the genus *Proteus*, were inoculated on to slopes of Kligler's iron agar, the medium being stabbed to the foot of the tube from the lower angle of the slope.

This method was preferred to the usual one of stabbing the butt from the centre of the slope, for two reasons: (1) the yellow reaction from a positive glucose dissimilation did not spread to the upper half of the tube; consequently no false positive lactose reactions occurred due to incomplete acid reversal on the slope; (2) the blackening of the medium due to the formation of hydrogen sulphide was similarly confined to the butt.

After stabbing, the slope was well streaked out to ensure maximal surface growth for the performance of the phenylalanine test.

The reactions in the Kligler's tubes were read after 18–24 hr. incubation at 37° C. and the cells from each slope were then washed off with 0·5 ml. of a 0·2 per cent L-phenylalanine solution in 0·1 molar phosphate buffer to *p*H 7·4, the cells being removed from the slope into the buffer solution by rubbing with a wire-loop, to obtain the heaviest suspension. This suspension was then poured into a bijou bottle and shaken for 10 min. on a 'Microid' flask shaker.

The shaking was then stopped, 0·1 ml. of an 8 per cent aqueous ferric chloride solution added to the suspension, and the bijou reshaken for 30 sec. or so.

An intense dark green colour was produced in the presence of phenylpyruvic acid. In every case only the *Proteus* strains gave this positive reaction. The other strains produced yellow or brownish reactions. The results obtained with the strains using the phenylalanine method of Buttiaux *et al.*[1] agreed entirely with these results.

The presence of sulphides in Kligler's medium did not interfere with either the performance or the reading of the test.

The advantage of using one medium for as many reliable tests as possible is obvious when one considers the increased risks of contamination involved in taking two 'picks' from any one colony on a selective plate, to inoculate two tubes of media.

To inoculate a separate slope for the phenylalanine test from a cultured Kligler slope means that there is an 18–24 hr. delay before a rapid phenylalanine test, such as Ben Hamida and Le Minor[5] suggested, can be carried out.

The extremely simple extension in the use of Kligler's medium outlined above to include the phenylalanine test should prove of value where speed of diagnosis is essential.

Other multiple sugar media could presumably be so utilized instead of that of Kligler.

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A Group of Pseudomonads able to synthesize Poly-β-hydroxybutyric Acid

POLY-β-HYDROXYBUTYRIC acid has been found to occur very infrequently in *Pseudomonas* although it is very common in the related genera *Chromobacterium*, *Spirillum* and *Vibrio*[1,2]. It is absent in authentic strains of *P. aeruginosa*, *P. fluorescens*, *P. aureofaciens*, *P. convexa*, *P. schuylkilliensis*, *P. pavonacea*, *P. lemonnieri*, *P. mildenbergii*, *P. syncyanea* and *P. chlororaphis*. Of classified strains tested it only appears to be present in the animal and the plant pathogens, *P. pseudomallei*[3] and *P. solanacearum*, which are scarcely typical of the genus. It has also been found in *P. antimycetica*[4] and a group of related organisms, which appear to be pseudomonads, referred to in previous publications[1,2] as "pseudomonads related to Hankey Culture Collection (HCC) B175". This group has now been studied in some detail and should, we feel, be considered members of *Pseudomonas*.

The strains were isolated mainly from Trinidad soils on glucose–'Marmite'–peptone agar plates. They form characteristic opaque yellow colonies which in some strains change after 2–3 days to an intense reddish-purple colour. They are all non-sporing, non-acid-fast, Gram-negative rods, 0·7–1·3μ × 0·4μ, occurring singly or in pairs; motile by means of a polar tuft of flagella varying from 3 to 8 in number. They are aerobic. They grow well at 37° C. and to some extent at 42° C. They will not grow below 15° C. All strains rapidly liquefy gelatin and peptonize milk. Citrates are utilized as the sole source of carbon. Neither indole nor acetoin is formed. Cellulose is not attacked.

The group is characterized by the production of massive inclusions of poly-β-hydroxybutyric acid on media containing a readily available energy source, and the production of a diffusible fluorescent pigment in asparagine–salts media[5] giving a violet fluorescence in ultra-violet light easily distinguishable from the bluish-green fluorescence of the normal fluorescent pseudomonads listed above. The strains all grow rapidly in a lactate salts medium. They have an oxidative metabolism[6] and rapidly oxidize glucose, sucrose and lactose. Their fermentative ability is weak—slight acid, no gas, from glucose but not from other sugars. They are strongly lipolytic. They hydrolyse æsculin but not starch.

They form two clearly defined sub-groups on the basis of pigment formation and nitrate reduction (Table 1).

Production of the purple pigment was examined. The best medium for pigment production was glycerol–peptone (2 per cent glycerol, 1 per cent peptone ('Oxoid'), 0·5 per cent sodium chloride, 0·1 per cent potassium nitrate). Strong aeration is essential. 1 litre of the above medium was inoculated with strain *B*175 and grown for three days in shake flasks. The purple pigment is insoluble in water and the usual organic solvents. The cells and pigment were therefore recovered by centrifuging and dried. The dried cells (about 10 gm.) were extracted with chloroform in a solvent extraction apparatus for 18 hr. The chloroform solution contained a small quantity of a yellow-green pigment and 3·1 gm. of poly-β-hydroxybutyric acid, m.p. 168° C. The residue was blended with 95 per cent ethanol containing 2 per cent v/v concentrated hydrochloric acid. This treatment causes the insoluble purple pigment to change to a yellow form soluble in organic solvents.

The purple form can be re-formed by making the solution alkaline. The alcohol extracts were concentrated to small volume and water added. The yellow pigment was extracted from the water layer with chloroform. The chloroform solution was chromatographed on silica gel, considerable dark-coloured material remaining adsorbed while pure pigment was eluted. The pigment was recrystallized from a benzene–*cyclo*hexane mixture as orange-yellow

Table 1

Strain		Source	Colour on glucose–'Marmite'–peptone–agar plate (5 days)	Nitrate reduction (5 days)	Growth at 37° C.	Growth at 42° C.
No.	Name					
1	*B*175	forest soil	dark red/purple	–	+++	+
2	Maraval	river water	red/purple	–	+++	+
3	*N.C.R.*	forest soil	brown/purple	–	+++	+
4	43	river water	purple	–	+++	++
5	*S*11*	soil	brown/purple	–	+++	++
6	Santa Cruz	cocoa soil	red/purple	–	+++	+
7	*N.C.R.*2	forest soil	yellow/purple	–	+++	+
8	*N.C.R.*3	forest soil	violet	–	+++	+
9	*N.C.R.*4	forest soil	violet	–	+++	+
10	*T*590	soil	red/purple	–	+++	+
11	*T*400	soil	red/purple	–	+++	+
12	Rupununi	savannah soil	yellow	+	+++	++
13	*T*277	heavy clay soil	yellow	+	+++	+
14	Centeno 6	savannah soil	yellow	+	+++	+++
15	Longdenville	citrus soil	yellow	+	+++	+
16	*T*456	soil	yellow	+	+++	++
17	Hololo	cocoa soil	yellow	+	+++	+
18	C.E.S.	savannah soil	yellow	+	+++	+

* This isolate has already been studied by Sneath (designated by him *T*1, ref. 7)

needles, m.p. 237–238° C. (2·5 per cent yield). (Found: C, 58·0; H, 3·8; O, 28·7; N, 8·5; OCH_3, 9·3; NCH_3, 8·9 per cent; molecular weight, 340. Calculated for $C_{1}H_{12}N_{2}O_{6}$: C, 58·5; H, 3·7; O, 29·2; N, 8·5; 1-OMe, 9·4; 1-NMe, 8·9 per cent; molecular weight, 329.) Hydrolysis of the pigment with 2 *N* sodium hydroxide for 20 hr. yielded a red acid, m.p. 284° C. Zinc dust distillation of this acid gave a yellow-brown distillate from which phenazine (identified by melting point and ultra-violet spectrum) was isolated by crystallization and sublimation. The original pigment depressed the melting point of an equal quantity of phenazine-α-carboxylic acid by 40 deg. C., indicating the non-identity of the two compounds. The absorption spectrum of the pigment differs markedly from the spectra of violacein, pyocyanin, chlororaphin, iodinin, phenazine-α-carboxylic acid[8], and the blue pigment from *P. lemonnieri*[9]. The chemical structure of this new phenazine pigment is being studied.

The organisms are therefore a group of Gram-negative, polar-flagellated rods of oxidative metabolism. They produce a diffusible fluorescent substance and the pigmented members produce phenazine pigments. Following Tobie[10], they should be included in the genus *Pseudomonas*.

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GENETICS and CYTOLOGY

Two New Basic Chromosome Numbers in the Musaceae

The scheme proposed by Cheesman[1], and now generally accepted, for the classification of the Musaceae depends partly on basic chromosome numbers. Two genera are recognized. The genus *Ensete* Horan. comprises species with monocarpic habit and $2n = 18$ chromosomes. Species of *Musa* L. form suckers more or less freely and are placed in four sections: Musa (Eumusa) and Rhodochlamys with $2n = 22$, Callimusa and Australimusa with $2n = 20$. This scheme includes nicely all the species thus far described, but among recent introductions to the Trinidad collections are two exceptional forms for which the classification will need to be elaborated.

Somatic chromosome counts were made from root tips by the method of Tjio and Levan[2].

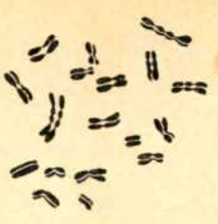

Fig. 1

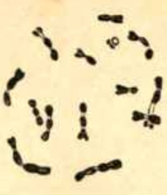

Fig. 2

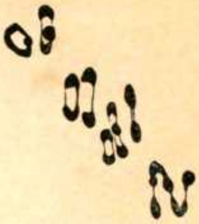

Fig. 3

Fig. 1. Somatic chromosomes of *I.R.* 503. (× 2,300)

Fig. 2. Somatic chromosomes of *I.R.* 510. (× 2,300)

Fig. 3. First meiotic metaphase in *I.R.* 503, showing a chain of four and seven bivalents. (× 2,300)

The first introduction, *I.R.* 503, is a seed collection from British North Borneo and is fairly certainly the unknown species noted by Simmonds[3], on the basis of herbarium material, as probably a new Rhodochlamys. Living plants, however, are more reminiscent of Callimusa; they differ from Callimusa spp. in seed characters and in the chromosome number, which is $2n = 18$ (Fig. 1). The second, *I.R.* 510, comes from the highlands of north-central New Guinea and is probably the largest herb in existence[4]. It has largish seeds, reminiscent of *Ensete*, but in some other respects resembles *Musa*. In its sparse suckering, especially if the leading stem is damaged, it is more or less intermediate between the two genera. The chromosome number is $2n = 14$ (Fig. 2). In neither case has the proper taxonomic position been decided, but at least one new section and perhaps a new genus can be envisaged. Indeed, it appears that a study of the wild bananas of the Indonesian area, still partly unknown, might enlarge the family considerably.

Only *I.R.* 503 has so far flowered in Trinidad and meiosis has been examined in acetocarmine smears of pollen mother cells of one plant. Chains of three or four chromosomes were seen at metaphase in occasional cells, indicating heterozygosity for a small translocation (Fig. 3). Structural diversity of this kind is frequently encountered in *Musa*. Translocation hybridity has been reported in cultivated clones of Eumusa, in hybrids between 22-chromosome species and in hybrids between geographical races of *M. acuminata*[5–7]. More recently, I have found (unpublished work) that homozygous translocations are distributed among the geographical sub-species and races of *M. acuminata* on a scale comparable with that found in *Gaillardia*[8], and have noted multivalents in several new crosses of 22-chromosome species and in one Australimusa hybrid. However, despite this high frequency of occurrence in edible bananas and in experimental hybrids, the present case is the first in which heterozygosity has been recorded in a wild collection. There is no evidence as to whether the translocation is a recent one or has been revealed by the mingling of already diverse populations.

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Feb. 2.

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Nuclear Fusion and Non-Fusion in *Theobroma cacao* L.

CYTOLOGICAL investigations carried out on *Theobroma cacao* have revealed the fact that the incompatibility reaction in this species is based on non-fusion between male gametes and female haploid nuclei carrying the same dominant S allele[1]. Incompatibility pollinated cacao ovaries contain approximately 25, 50 or 100 per cent of ovules wherein fusions between the first male gamete and the egg nucleus and between the second male gamete and the polar nuclei have not taken place. In such ovules, the egg and male nuclei appear always to lie in actual contact, each preserving its spherical shape; the second male gamete and the polar nuclei, however, do not show such regularity of behaviour, for the two polar nuclei may sometimes become dissociated from one another, the male nucleus lying elsewhere in the embryo-sac or in contact with one of the separated polar nuclei.

When fusion does take place between a male gamete and the polar nuclei, the male gamete invariably places itself at some point on the line of juncture of the two polar nuclei, so that the male nucleus lies in simultaneous contact with both female nuclei before fusion takes place. The male gamete appears not to fuse at random over the surface of one or other of the polar nuclei but always comes into the position where all three nuclei are in mutual contact. The male nucleus then insinuates itself between the polar nuclei, assuming a more and more fusiform shape as it penetrates. Finally, the contents of the male nucleus mingle with the nucleoplasm of one of the polar nuclei. The process is shown in diagrammatic form in Fig. 1.

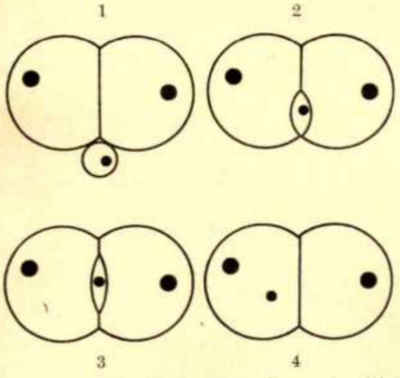

Fig. 1. Four stages in the fusion of a male gamete with the polar nuclei in cacao (diagrammatic)

This fusion behaviour can be likened to the coalescence of oil droplets in an extremely unstable oil/water emulsion; here the fusing oil droplets tend to share large areas of their surfaces and hence assume a polyhedral form[2]. The male nucleus, originally spherical (as is a single oil droplet), arranges itself between the polar nuclei in such a manner that its entire surface is shared with these two nuclei. Fusion with one or other polar nucleus is a purely random process.

In the case of non-fusing nuclei, entirely different interfacial conditions must exist and the system can be likened to a stable oil/water emulsion in which no coalescence of the oil droplets takes place. In emulsions stabilized, for example, with a protein, direct oil-to-oil contact between droplets is prevented by the presence of a monolayer of adsorbed protein at the surface of each droplet. This condition does not imply that the stabilized droplets cannot make contact, but rather that when contact is made they preserve their spherical form. Clusters of spherical oil droplets can be seen under the microscope in many emulsions.

The not infrequent separation of the two polar nuclei in ovules showing non-fusion leads us to suggest that this effect is brought about by the presence of a strongly but specifically adsorbed substance in the cytoplasm of the male nucleus carrying the dominant S allele. When both male and polar nuclei carry the same dominant allele (for example, S_1 nuclei in in $S_{1\cdot 2}$ selfed or in $S_{1\cdot 2} \times S_{1\cdot 3}$), the substance which 'interferes' with nuclear fusion diffuses from the male cytoplasm into that associated with the polar nuclei, from which it interacts with specific sites on the surface of both polar nuclei, leading to protection against fusion (or stabilization of all three bodies). In these circumstances the separation of the nuclei is understandable.

No specific adsorption sites, apparently, are present at the surface of polar nuclei which carry the recessive allele (for example, S_2 nuclei in the $S_{1\cdot 2}$ genotype) for fusion with any male nucleus will always take place. When the polar nuclei carry a dominant S allele different from that of the male gamete, fusion again will ensue; for example, S_3 polar nuclei in an $S_{3\cdot 4}$ genotype will fuse with S_1 male gametes derived from an $S_{1\cdot 2}$ genotype because the S_3 sites are not specific adsorption sites for the S_1 protective substance. If the male nucleus does not carry a dominant S allele, no protective substance is present in its cytoplasm; it will therefore always fuse with any female nuclei.

In view of the specificity of the non-fusion reaction, the protective substance is likely to be proteinaceous in character.

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Genetics of Dieldrin Resistance in *Lucilia cuprina* Wied.

IN a comprehensive paper on insecticidal resistance in anopheline mosquitoes Davidson[1] demonstrated that resistance to dieldrin in *Anopheles gambiae* is due to a single gene, partially dominant. In this work the discriminating dose technique, supported by Milani[2], for genetical studies on insecticidal resistance in insects was utilized.

Employing this method in a study of the genetics of dieldrin resistance in *Lucilia cuprina*, in which insecticidal resistance has been demonstrated[3], it is indicated that dieldrin resistance in this insect is also due to a partially dominant single gene. To date information is available only from a cross between susceptible female flies and a single resistant male fly. The results, however, conform so closely to a Mendelian interpretation on a single gene basis that it can be expected that additional work will merely confirm the above conclusion.

In this preliminary study a single resistant male fly, which survived 4 μgm. of dieldrin, was crossed with ten susceptible female flies. The male fly was taken from a strain of flies undergoing selection in an attempt to develop a homogeneous strain of blowflies for genetical studies.

The male and female $F1$ progeny of the initial cross were intermediate in resistance. A dosage of 0·1 μgm. dieldrin/fly (the dose which consistently kills all susceptible flies) gave no mortality, while 4 μgm. dieldrin/fly gave complete mortality. Application of the discriminating dose (0·1 μgm. dieldrin/fly) on both males and females of the $F2$ resulted in close agreement with a 1 : 3 ratio (1 dead : 3 alive). The tests were made on 1,007 flies. The above ratio applied more closely to female than male flies.

In the back-crosses an approximate 1 : 1 ratio and complete survival resulted when the discriminating dose of 0·1 μgm. of dieldrin was applied to the progeny of $F1$ females × susceptible male (287 flies) and $F1$ females × resistant male (136 flies) respectively. Flies of both sexes were again treated.

The insecticide, dissolved in kerosene, was applied topically with a micro-applicator which delivered 0·5 μl./fly.

Thanks are due to Dr. J. R. Busvine of the London School of Hygiene and Tropical Medicine and R. Milani of the Zoological Institute, Pavia, Italy, for suggestions regarding this work. Acknowledgment is also made of assistance given by R. Hart of Geigy A/Asia (Pty.) Ltd.

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Sydney. March 4.

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Amounts of Deoxyribonucleic Acid in the Silk Glands of the Spider *Nephila maculata*, Fabr., 1763

THE major chemical components of a chromosome so far described are two types of protein and deoxyribonucleic acid. The amounts of the two types of chromosomal protein vary considerably between the tissues of one animal[1]. Deoxyribonucleic acid content is much less variable, however, and appears[2-4] to be approximately constant in the nuclei of the same species. However, recent work by Leuchtenberger and Schrader[5] indicates that the quantities are likely to vary in secretory tissues.

In the course of this investigation the silk glands of *Nephila maculata* were selected for analysis. There are five types of silk glands in this spider, namely : (1) aggregate glands ; (2) ampullate glands ; (3) cylindrical glands ; (4) aciniform glands ; and (5) pyriform glands. All these glands are highly secretory and are concerned with the production of silk for the construction of the web.

The tissues were removed from freshly killed animals as quickly as possible and were fixed in Carnoy's acetic alcohol (3 parts of absolute alcohol : 1 part of glacial acetic acid). The fixation period was usually 4 hr. The fixative was then thoroughly washed off the tissues, which were then embedded in paraffin, cut at varying thickness, and stained with Feulgen stain as described by Stowell[6].

Measurements were made on an apparatus similar to that described by Pollister and Moses[7], with an *RCA* 931*A* electron multiplier phototube and a light source consisting of a tungsten ribbon filament lamp, from which the 546-mμ wave-length was isolated by the Farrand interference filter (peak 550 mμ) to estimate the Feulgen reaction. Readings were taken on a 'Rubicon' galvanometer. The final values in arbitrary units were obtained as described by Swift[8].

Table 1

Cell type	No. of nuclei measured	Volume of nuclei (μ^3)	Deoxyribonucleic acid (arbitrary units)
Aggregate gland	49	36·810 ± 11·453	2·339 ± 0·444
Ampullate gland	49	44·525 ± 15·058	2·495 ± 0·477
Cylindrical gland	49	29·981 ± 6·082	2·475 ± 0·397
Aciniform gland	49	31·535 ± 6·260	2·435 ± 0·461
Pyriform gland	50	42·662 ± 13·23	2·891 ± 0·595

Table 1 gives the results obtained by photometric estimations.

It will be seen that there is considerable variation in the volume of the nuclei from different silk glands. Even in the nuclei of the same gland the deviation is quite significant. This is indicative of the differential secretory activity in the nuclei, as the volume of the nuclei will be directly related to the accumulation of the products of secretion liberated into the cytoplasm. On the other hand, the quantities of deoxyribonucleic acid are remarkably constant not only in the nuclei of the same gland but also in the nuclei of the different glands. This indicates that the quantities of deoxyribonucleic acid are not directly related to the secretory activity of the nucleus. This finding is in agreement with the hypothesis of constancy, but differs from the observations of Leuchtenberger and Schrader[5], who find that the quantities of deoxyribonucleic acid in *Helix*, though generally constant in body tissues, are likely to vary in secretory tissues. The decrease of deoxyribonucleic acid in the nuclei of the salivary gland of *Helix* is, according to Leuchtenberger and Schrader, the result of its utilization in the formation of secretory products in the cytoplasm. In *Nephila*, however, the amount of deoxyribonucleic acid is constant and does not bear any direct relation to the secretory activity.

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HYDROLOGY

Marine Studies in the Inshore Waters of Antarctica near Mawson, 1956

THIS investigation, aimed at obtaining information concerning the hydrology and biology of the inshore waters of Antarctica, especially during the winter period, formed part of the scientific programme of the 1956–57 Australian National Antarctic Research Expedition to Mawson (67° 31′ S. lat., 62° 53′ E. long.) in MacRobertson Land. After a period of establishment, I began regular observations in June and continued at weekly intervals until February

1957. Two stations were occupied, one in 25 m. and the other in rather more than 100 m. of water. Observations were made at various depths throughout the water column. For the greater part of the period the surface was frozen to a maximum recorded depth in September of 115 cm. Water samples were taken in the normal manner with Nansen bottles but using modified operating techniques to meet the severe conditions. Plankton hauls, mainly vertical and entailing considerable difficulty, were run with $N50$ and $N70$ nets.

From the water samples, and in addition to records of temperature, measurements were obtained of pH, E_h, buffer capacity, dissolved phosphates and oxygen, and chlorinity. Measurements of submarine solar radiation were taken down to a maximum depth of 10 m. A high-speed continuous centrifuge was used to extract phytoplankton both for the determination of chlorophyll and for qualitative and quantitative examination.

Although the results are too extensive to be described in detail in this communication, it may be of interest to indicate briefly some of the features of particular interest. Chlorinity values obtained during winter were low, mean figures ranging from $16{\cdot}00$ to $18{\cdot}70\,^{0}/_{00}$. These chlorinities, combined with mean temperatures between −1·90° C. and −1·60° C., commonly produced freezing conditions extending well down into the water column and appeared to cause the formation of ice crystals in free suspension, apart from the sea ice formed at the surface. Chlorinities were appreciably higher during summer except for a temporary shallow surface zone of extremely low salt content produced by the melting of the sea ice. Evidence was obtained which indicates a process by which the summer waters undergo incomplete mixing and remain close to the coastline until their replacement by relatively homogeneous water of higher chlorinity with the onset of the following summer.

As might be expected in these latitudes, the incidence of submarine solar radiation was found to exhibit marked seasonal differences, being negligible during the long winter period partly because of the low elevation of the Sun and partly because of the highly reflecting layer of sea ice. Consequent upon such conditions, phytoplankton was virtually absent during the winter period although small numbers of zooplankton organisms were taken in the nets. It is of interest that phytoplankton appeared and began to increase and attached diatoms were found actively growing on the under surface of the sea ice while the ice itself was more than 100 cm. thick. Large-scale blooms did not occur, however, until the ice was in an advanced stage of disintegration during the thaw.

The striking qualitative differences between the phytoplankton extracted with the continuous centrifuge and that taken with the nets was particularly illuminating, especially as the greater part of the chlorophyll estimated must have been contributed by forms either rare or absent in the material gathered by conventional methods. Based on chlorophyll concentrations, it was estimated that the carbon content in the standing crops of summer phytoplankton lay between $0{\cdot}30$ and $14{\cdot}80$ mgm./m.^{3}.

Full details of the above investigation will be published elsewhere.

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ARCHÆOLOGY

Apple-Scoops

Being a private collector of items relating to bygone dentistry, I was naturally interested to read Prof. Raymond A. Dart's communication (*Nature*, March 21, p. 844) on "An 'Australopithecine' Scoop from Herefordshire".

Apple-scoops (occasionally termed gouges) were freely used in apple-growing districts by edentulous persons to scrape small thin pieces off the fruit and thus facilitate mastication. This custom was particularly prevalent prior to the introduction into Great Britain, in 1855, of vulcanite as a base for artificial dentures. Until then, such restorations were expensive due to the time and labour necessary to carve them from hippopotamus or walrus tusks with the precision that would ensure an accurate fit: the alternative being natural or ivory teeth attached to a swaged gold foundation.

The most popular apple-scoops were undoubtedly home-made and fashioned from the metacarpus or metatarsus of sheep. Others were constructed of ivory. A silver (Birmingham hallmark 1830) specimen, which I possess, unscrews from its hollowed ivory handle and fits into this for portability. Incidentally, there is a small but very comprehensive collection of apple-scoops in the Folk Museum, Gloucester.

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METALLURGY

Ductile Cleavage Fracture of Molybdenum

Most metals other than those having a face-centred cubic structure show a more or less rapid transition from ductile to brittle behaviour as the temperature is lowered. Well above the transition temperature the fracture surfaces are mainly fibrous with only a few cleavage facets, but at intermediate temperatures fracture occurs by cleavage after a strain of a few per cent. So far little attention has been paid to the mechanism of this ductile cleavage fracture. Recently, we have examined cleavage facets and longitudinal sections of a number of fractured specimens in which cleavage occurred after straining about 10 per cent at room temperature at a rate of strain of $0{\cdot}88 \times 10^{-4}$ sec.$^{-1}$. The tensile specimens, which had grain diameters of about 2 mm., were prepared from arc-cast deoxidized molybdenum and were 0·1 in. in diameter[1]. The results throw some light on the mechanism of fracture.

Part of a typical fracture edge is shown in Fig. 1. It is made up mainly of straight-line segments which often occupy one complete grain (see *A* in Fig. 1). Within about 0·5 mm. of each fracture edge a number of subsidiary cracks are observed (see *B* in Fig. 1) and often these are arranged in a characteristic configuration, an example of which is shown in Fig. 2. The cracks do not cross grain boundaries and those making up a configuration are always contained in one grain. Occasionally an 'ear', such as that shown at *C* in Fig. 1, is observed on the edge of the fracture. Such ears have been shown to be the result of the joining of two overlapping cracks on different cleavage planes by the shearing of the material

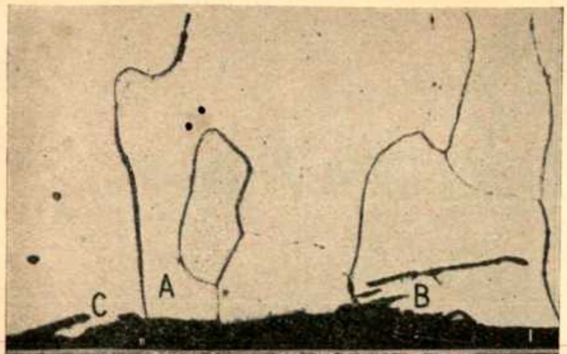

Fig. 1. Longitudinal section through the fracture surface of a molybdenum specimen which fractured after 10 per cent strain at room temperature. (× 250)

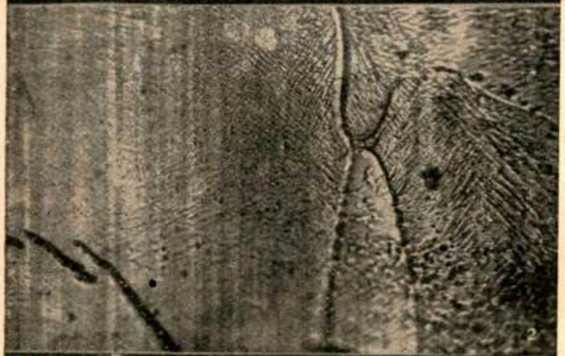

Fig. 2. A similar specimen to that of Fig. 1, but electro-etched, showing wavy slip lines and 'forced slip' near the grain boundaries. (× 250)

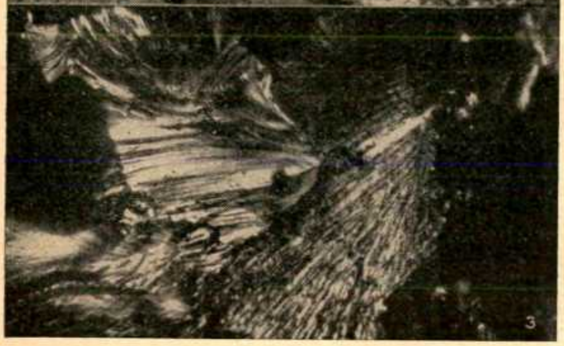

Fig. 3. Photograph of some cleavage facets on the fracture surface of a specimen similar to those shown in Figs. 1 and 2. (× 250)

between them[2]. The markings on the cleavage facets (Fig. 3) suggest that the growth directions are different for each crack.

We believe that these results show that fracture occurs by the joining of many cracks which grow co-operatively in a narrow band across the specimen. The grain boundaries provide barriers which are sufficient to prevent their propagation, and the final stage of the fracture is one of shearing at or near the grain boundaries to form the complete fracture surface. Some of the cracks are not needed to form the fracture surface, and these are left after fracture as subsidiary cracks such as those in Figs. 1 and 2. The existence of configurations of cracks such as that in Fig. 2 shows that cracks can occur on more than one crystallographic plane, even within one grain.

The wavy slip lines shown in Fig. 2 were revealed by electro-etching and are characteristic of body-centred cubic metals. Near the grain boundaries, 'forced slip' has occurred on intersecting slip systems and this would be expected to increase still further the difficulty of propagating a crack through a grain boundary.

A more detailed study of this type of fracture is being made and will be reported elsewhere. The work is being carried out while one of us (A. A. J.) is holding a University of London I.C.I. Research Fellowship and the other (B. J. S.) a U.K. Atomic Energy Authority Research Bursary.

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March 14.

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A New Silicide in a 12 per cent Chromium Steel

In the course of an investigation into the tempering characteristics of a 12 per cent chromium steel (C 0·098, Mn 3·18, Si 3·02, Ni 4·06, Cr 12·56, Mo 0·49, V 1·09 per cent) a new phase was discovered. This phase (which we have called *H*-phase) could not be obtained in isolation but was always associated with $M_{23}C_6$. A residue extracted after tempering the steel for 50 hr. at 750° C., however, gave the maximum proportion of the new phase to $M_{23}C_6$. This was of the order of 2 : 1. This residue was examined in more detail by X-rays and a full chemical analysis was obtained.

The specimen was photographed in a 9-cm. diameter powder camera and a quadruple focusing camera, cobalt $K\alpha$ radiation being used in both cases. The interplanar spacings of the new phase fitted a cubic lattice with $a = 10{\cdot}735$ kX. The interplanar spacings are listed in Table 1, together with line intensities and indices. The X-ray pattern of the new phase shows marked resemblances to the pattern of M_6C. The space group of the new phase is probably *Fd*3*m*.

The full chemical analysis, converted to atomic percentages, is shown in Table 2. Due to the presence of $M_{23}C_6$ it is very difficult to form any definite conclusions about the composition of the new phase

Table 1. X-Ray Data for *H*-Phase ($a = 10{\cdot}735$ kX.)

Intensity	$h^2 + k^2 + l^2$	Corrected *d*	Observed *d*
vw*	11	3·237	—
vw*	12	3·099	—
vw*	16	2·689	—
vw	19	2·463	2·439
wm	24	2·191	2·176
s	27	2·066	2·051
wm	32	1·898	1·887
wm†	36	1·789	1·782
vw	44	1·618	1·612
w	51	1·503	1·497
w	59	1·398	1·394
vw	67	1·311	1·307
ms	72	$1{\cdot}265_1$	$1{\cdot}261_8$
wm	75	$1{\cdot}239_6$	$1{\cdot}235_9$
vw	84	$1{\cdot}171_3$	$1{\cdot}169_1$
m	99	$1{\cdot}078_9$	$1{\cdot}078_0$
wm	104	$1{\cdot}052_7$	$1{\cdot}051_9$
w	107	$1{\cdot}037_8$	$1{\cdot}037_1$
w	108	$1{\cdot}033_5$	$1{\cdot}031_7$
w	123	0·9679	0·9680
vw	132	0·9344	0·9342
wm	136	0·9205	0·9204

* Detected on the focusing camera film only.

† Interference due to an $M_{23}C_6$ line.

Table 2. ANALYSIS OF A MIXTURE OF *H*-PHASE AND $M_{23}C_6$ (IN THE APPROXIMATE RATIO OF 2 : 1)

Element	Atomic weight
C	8·8
N	2·8
Mn	0·8
Ni	4·0
Cr	18·8
Mo	1·2
V	8·2
Fe	20·8
Si	34·6

but the large amount of silicon is significant. After allowing for the $M_{23}C_6$ the new phase appears to be a silicide of formula MSi_x, where M stands for Fe, Cr, V, Ni and Mo, and x is probably greater than 1.

The full elucidation of the composition and structure of this phase must await further attempts to isolate or synthesize it.

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PHYSICAL SCIENCES

An Effect of Oxide Layers on the Behaviour of Vacuum Arc Cathode Spots

IN the course of a preliminary experiment to study the effect of electrode surface condition on the behaviour of the cathode spot of a d.c. vacuum arc an interesting phenomenon was observed.

The surface of a vacuum-cast copper cathode was prepared by abrasion on emery paper and hand polishing on a 'Selvyt' cloth. After degreasing in a petroleum ether still, the surface was cathodically etched in argon and the grain boundaries were clearly revealed. The surface was then oxidized to cuprous oxide by heating in air.

The d.c. arc discharge was struck by touching a pointed tungsten anode on to the prepared surface, both electrodes being mounted in a glass vacuum chamber exhausted to 0·01μ mercury pressure. A mechanical switch shorted the arc after 20 millisec.

The cathode spots left characteristic continuous tracks on the electrode surface, and it was found that the markings were absent from certain grains as shown in Fig. 1. The characteristic tracks stop abruptly at the grain boundaries and it appears that the cathode spot is able to operate more easily on some grains than others, and a definite preferential action was observed.

This effect occurred when the current flowing before the electrodes were separated was 5 amp., and did not occur when the arc current was greater, for example, 50 amp. short-circuit current.

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Manchester 17.
March 24.

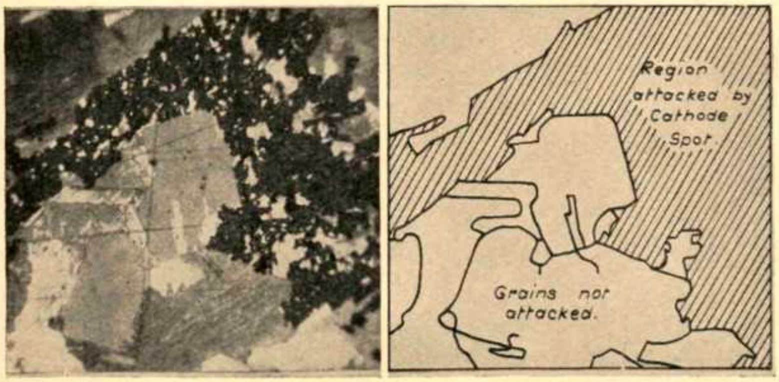

Fig. 1. Copper cathode, etched and oxidized, after attack by cathode spot. (× c. 62)

The λ-Transition in Helium

RECENT experiments on the inelastic scattering of neutrons by superfluid helium[1,2] have given a direct confirmation of the correctness of the elementary excitation spectrum (rotons and phonons) of Landau's theory[3]. As it is usually formulated, the theory postulates that the excitation spectrum is independent of temperature. However, the velocity of sound is known to vary somewhat with temperature[4], and the neutron scattering experiments[1] show an appreciable fall in the minimum roton energy Δ, as the temperature approaches the λ-point.

It is possible to understand the non-existence of superfluidity above the λ-point if one has reason to believe that Δ vanishes at the λ-point[5]. But if Δ really were to vanish at the λ-point, it would almost certainly imply the existence of an Ehrenfest[6] second-order transition, that is, a finite discontinuity in the specific heat. Recent measurements of the specific heat of liquid helium[7] show a more complicated anomaly—a finite discontinuity is superimposed on a logarithmic infinity.

A phenomenological model can easily be constructed for the dependence on temperature of Δ, leading to a specific heat anomaly of the kind observed, while agreeing closely with the observed $\Delta(T)$ within the temperature region covered by the neutron scattering experiments[1]. One such model for $\Delta(T)$ is :

$$\left.\begin{aligned} \Delta &= \Delta_0, & \xi &< -1 \\ &= \Delta_0(|\xi| + \xi\ln|\xi| + e^{-2})/(1 + e^{-2}), & -1 < \xi &< e^{-2} \\ &= 0, & \xi &> e^{-2} \end{aligned}\right\} \quad (1)$$

where

$$\xi = \alpha(T/T_\lambda - 1), \quad (2)$$

and the constant of proportionality α is to be chosen to give the best fit with experiment.

Fig. 1 illustrates the postulated behaviour of Δ (where the scale factor α in equation (2) has been put equal to 4); for comparison the experimental points of Larsson and Otnes[1] are also shown. The specific heat anomaly arises from the singularity in $d\Delta/d\xi$ at $\xi = 0$. This derivative has a finite discontinuity and a logarithmic infinity, and the ratio of the coefficient of the logarithm to the magnitude of the discontinuity is $\frac{1}{2}$. The experimental value[7] of this ratio is $\sim 0{\cdot}3$.

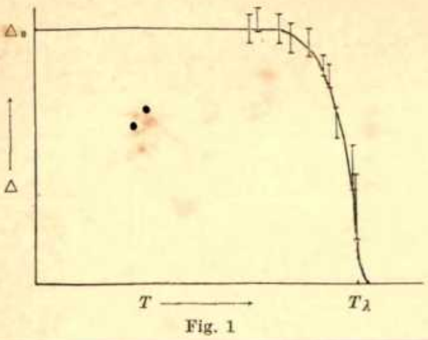

Fig. 1

If this phenomenological model has any significance, it implies that Δ does not vanish at the transition, but falls rapidly to zero for values of ξ slightly greater than zero (up to $\xi \sim 0\cdot 1$). It might be hoped that inelastic neutron scattering experiments in a temperature region containing the λ-point (say, 2·0 to 2·3° K.) could test the present suggestion; unfortunately the results reported suggest that the line width becomes prohibitively great near the λ-point.

The form of $\Delta(\xi)$ may well be more complicated than is proposed here—equation (1) has discontinuous second derivatives at $\xi = -1$ and at $\xi = e^{-2}$ which would give spurious Ehrenfest third order transitions at these temperatures. If Δ is indeed finite above the λ-point, then the value of Δ can fulfil the role of the short-range order parameter in an order–disorder transition. The absence of superfluid behaviour immediately above the λ-point will, however, require a separate explanation, and may possibly be linked with the increasing line-width for neutron scattering.

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Townsend's First Ionization Coefficient in Pure Nitrogen

With equipment assembled for the measurement of Townsend's α in highly pure hydrocarbon gases, it was thought interesting to carry out preliminary but careful measurements in a common diatomic gas. Now that satisfactory agreement has been reported for hydrogen[1,8] which does not depend too critically on purity, it was hoped to confirm the latest results in pure nitrogen obtained by Harrison[2], which differ from all other workers (and those to be presented here) by up to an order of magnitude.

Previous results[3–8], corrected to 0° C., are shown in Fig. 1. Excepting the values of Ayers[3], overall agreement is reasonable (within 30 per cent, later results agreeing better) considering the unspecified nature of possible contaminants present in each case. As a reference, the values of Masch will be used[4] because, among other reasons to be given, his results provide a consistent set of values taken over a wide pressure range and cover the whole E/p_0 region under consideration. Bowls's[6] values, though obtained with a mercury-free system, only cover the higher E/p_0 region.

As shown, Harrison obtained values for (*a*) 99·99 per cent nitrogen, obtained from sodium azide; (*b*) 99·9 per cent purified cylinder nitrogen (0·06 per cent oxygen, 0·04 per cent argon, obtained by passing gas (*c*) through hot copper and a liquid nitrogen trap); (*c*) 99·9 per cent cylinder nitrogen. His results indicate that: (1) the presence of 0·1 per cent of common impurities such as oxygen or argon lowers α/p_0 by from 30 to 3 per cent; (2) the presence of a further $\simeq 0\cdot 1$ per cent of some other contaminant found in cylinder nitrogen and removed by liquid nitrogen lowers α/p_0 by another 35 per cent. These rather large effects would satisfactorily account for previously found discrepancies and would indicate that Masch's results should compare favourably with Harrison's (*a*) curve. Comparing the absolute magnitude of these two sets of results, however, reveals a discrepancy by a factor of 2–10; even using Harrison's (*c*) results still gives a discrepancy of 2–6 times. A shift in the E/p_0 axis of about 10 would give almost perfect agreement all round.

Values of mine obtained in 99·998 per cent nitrogen are also shown in Fig. 1 (impurities: $O_2 < 10$ vol./million; $CO_2 < 5$ v./m.; $H_2 < 1$ v./m.; $A \leqslant 5$ v./m.; gas supplied by B.O.C. Ltd.). These were obtained in a $\frac{3}{4}$-litre system incorporating ultra-high vacuum techniques and which will be described elsewhere. To make optimum use of the variable 0·2–1·2 cm. parallel-plate gap, the pressure of the samples covered 50–400 mm. mercury. Mercury contamination was completely eliminated using a differential pressure device. Conditions were such that no impurity greater than that originally present

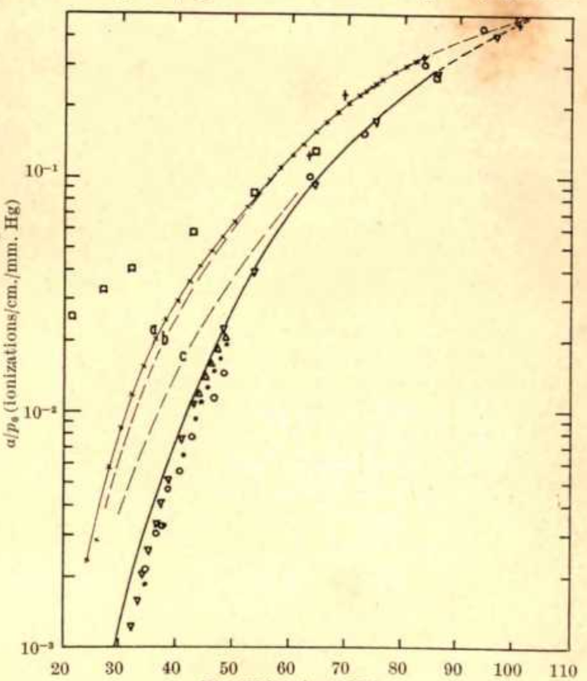

Fig. 1. Full curve, present work; □, Ayers; ▽, Masch; ○, Posin; +, Bowls; △, Dutton, Haydon and Llewelyn Jones; ●, de Bitetto and Fisher; ×, Harrison (*a*, *b*, *c*)

in the sample could possibly have been added. The use of a liquid-nitrogen trap in the gas supply line did not affect the results.

It is seen that the curve coincides with the values of Masch except at very low E/p_0. This agreement may seem surprising as the results of Masch were obtained in 99 per cent nitrogen in a mercury-contaminated system, which it is known increases the α/p_0 values. Although the presence of an impurity, as shown above, becomes more marked as E/p_0 decreases, the experimental means of obtaining these lower E/p_0 values necessitates for any particular system a corresponding use of increased gas pressures. In the case of Masch this pressure increase was exceptional, as he used a 6-mm. maximum gap. Thus, at $E/p_0 \simeq 100$, $p_0 \simeq 10$; at $E/p_0 \simeq 50$, $p_0 \simeq 700$ and at $E/p_0 \simeq 30$ a pressure of 2,000 mm. mercury was employed. At these pressures the effect of the presence of mercury should be small to negligible. A sharp break in the results of Posin[5] at $E/p_0 = 54$ at which the pressure employed was increased from 1 to 100 mm. mercury can also be attributed to the reduced effect of mercury contamination in the lower E/p_0 region. To check his gas samples Masch tested nitrogen obtained from sodium azide (as for Harrison's (*a*) curve) and could detect no difference.

Results obtained by N. J. Peacock (private communication) for 99·9 per cent cylinder nitrogen in a system with which excellent agreement was obtained for 99·95 per cent hydrogen[9], also agree with Masch's values and coincide with the present results. This agreement is important, as it enables α values obtained in necessarily large systems as a preliminary to the investigation of secondary processes to be used with confidence.

Thanks are due to Prof. M. W. Humphrey Davies for facilities provided. This work was carried out during the tenure of an Imperial Chemical Industries Fellowship, which is gratefully acknowledged.

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Rise and Decay of Intensity of Luminescence of Short-Persistence Phosphors

RECTANGULAR-WAVE cathodo-excitation of short-persistence phosphors is known[1] to produce curves of intensity of luminescence of the shape indicated in Fig. 1, the sections of rise and decay each being represented by the sum of two characteristic exponential functions. These may be expressed, with the notation of Fig. 1, for the rise by:

$$L_r/L_e = 1 - [k_{r_1} \exp(-t/\tau_{r_1}) + k_{r_2} \exp(-t/\tau_{r_2})] \quad (1)$$

and for the decay, provided that the steady-state condition L_e has virtually been attained at $t < t_p$, by:

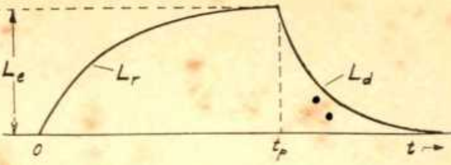

Fig. 1. Pulse of luminescence of short duration with rectangular-wave excitation

$$L_d/L_e = k_{d_1} \exp[-(t-t_p)/\tau_{d_1}] + k_{d_2} \exp[-(t-t_p)/\tau_{d_2}] \quad (2)$$

where $k_{r_1} + k_{r_2} = k_{d_1} + k_{d_2} = 1$, and $\tau_{r_2} \ll \tau_{r_1}$, $\tau_{d_2} \ll \tau_{d_1}$.

The short-period rise and decay of intensity of luminescence in phosphors of the respective types are commonly explained in terms of the random time an electron of a luminescence centre spends in an excited state. So far, no explanation appears to be available for the co-existence of the two exponential processes, with $\tau_2 \ll \tau_1$, during rise and decay.

The phenomenon that $\tau_2 \ll \tau_1$ may possibly be interpreted as the effect of a difference in the structures of luminescence centres, depending on whether they are situated in the body of a phosphor crystal or at, or near, its surface, and resulting in a considerable difference in the respective average time which an electron spends in an excited state. Measurements with phosphors of different crystal-sizes are to be made in order to clarify this question.

The rise and decay characteristics of the intensity of luminescence of the following short-persistence cathode-ray tube phosphors have been determined:

Phosphor *A*: ZnS: 0·005 per cent Ag
Phosphor *B*: ZnS: 0·005 per cent Ag: 0·0005 per cent Ni
Phosphor *C*: ZnS: 36 per cent CdS: 0·017 per cent Ag

(The phosphors were supplied by Derby Luminescents, Ltd.) Their spectral emission characteristics have the usual bell-shaped form with the peak at $\lambda = 0{\cdot}46\mu$ for phosphors *A* and *B*, and at $\lambda = 0{\cdot}525\mu$ for *C*. The phosphors were laid as screens in aluminized cathode-ray tubes of the flash-tube type[2], which were operated at an accelerator voltage of 15 kV. with rectangular-wave beam-current pulses of 30 μsec. duration at a frequency of 50 pulses/sec., the whole screen area of a tube being excited simultaneously and at a uniform density. The variations of intensity of luminescence were picked up with an electron-multiplier photovalve responding to radiation with $0{\cdot}30\mu < \lambda < 0{\cdot}65\mu$, and recorded with a high-speed recurrent-transient oscillograph.

The measurements were made for different values of electron beam density, J_b, and with the spectral response of the photovalve (*a*) corrected to that of the photometric standard observer for photopic vision, that is, eye correction, and (*b*) modified with a Chance *OX*7 filter so that the photovalve responded only to any ultra-violet radiation with $0{\cdot}30\mu < \lambda < 0{\cdot}43\mu$ transmitted through the cathode-ray tube face. The results are given in Table 1, the coefficients k and time constants τ relating to equations 1 and 2. The values of k_{r_1} and k_{r_2}, and of τ_{r_2} (see equation 1) are not given in Table 1, because they could not be determined accurately due to the fact that the beginnings of the rising curves were not accurately recorded with the existing equipment.

The results in Table 1 confirm[1] that $\tau_{d_2} \ll \tau_{d_1}$, and that increasing J_b tends to reduce the values of τ_{d_1} and τ_{d_2}. In addition, it is to be noted that (*a*) in all cases we have $\tau_{d_1} < \tau_{r_1}$, and (*b*) the values of τ

Table 1

Phosphor	J_b (m.amp./cm.^{2})	Visible radiation					Ultra-violet radiation				
		τ_{r_1} (μsec.)	kd_1	τd_1 (μsec.)	kd_2	τd_2 (μsec.)	τ_{r_1} (μsec.)	kd_1	τd_1 (μsec.)	kd_2	τd_2 (μsec.)
A	8·0	10·0	0·80	4·8	0·20	0·4	7·0	0·80	4·2	0·20	0·2
	2·0	11·2	0·80	7·0	0·20	0·5	10·0	0·80	5·2	0·20	0·2
B	5·0	8·5	0·88	5·5	0·12	1·0	4·5	0·80	4·0	0·20	0·4
	1·25	11·5	0·88	7·0	0·12	1·1	10·0	0·80	4·2	0·20	0·4
C	8·0	6·0	0·80	5·5	0·20	0·3	2·5	0·80	2·0	0·20	0·2
	3·0	10·0	0·80	7·0	0·20	0·5	7·0	0·80	5·5	0·20	0·9

for ultra-violet radiation are smaller than the corresponding values for visible radiation.

The difference in the values of τ for ultra-violet and visible radiations indicates a difference in the average time an electron spends in an excited state. It may perhaps be concluded that the difference depends on the height of the energy-level of the excited state and hence the magnitude of the energy-jump of the electron when returning to the ground-state, a higher energy-level being associated with a shorter average time in the state of excitation, and vice versa. This point is to be investigated in more detail.

The observation that $\tau_d < \tau_r$ contradicts existing theoretical considerations[1], according to which the time constant for rise should be smaller than that for decay.

Take approximations for the luminescence intensity curve (Fig. 1). Then for a rise in luminescence:

$$L_r/L_e = 1 - \exp(-t/\tau_r) \tag{3}$$

and for decay, with L_e independent of t_p,

$$L_d/L_e = [1 - \exp(-t_p/\tau_r)]\exp[-(t-t_p)/\tau_d] \tag{4}$$

The energy, W_r, stored in excited electrons during the rise is, from equation 3 and with a proportionality factor A,

$$\begin{aligned} W_r &= A\int_0^{t_p}(L_e - L_r)\,\mathrm{d}t \\ &= A\,L_e\,\tau_r[1 - \exp(-t_p/\tau_r)] \end{aligned} \tag{5}$$

The energy, W_d, converted from excited electrons to luminescent radiation during decay is, from equation 4:

$$\begin{aligned} W_d &= A\int_{t_p}^{\infty} L_d\,\mathrm{d}t \\ &= A\,L_e\,\tau_d\,[1 - \exp(-t_p/\tau_r)] \end{aligned} \tag{6}$$

From equations 5 and 6:

$$\tau_d/\tau_r = W_d/W_r \tag{7}$$

Because of non-radiative dissipation of energy of excited electrons when returning to the ground-state, we have $W_d < W_r$, and thus from equation 7 that $\tau_d < \tau_r$, which is in accordance with experimental evidence.

The magnitude of the ratio τ_d/τ_r is governed by the magnitude of non-radiative dissipation of energy and is therefore a measure for the probability of non-radiative return of an excited electron to the ground-state.

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Estimation of Chain Fracture during the Cross-linking of Rubber Hydrocarbons by High-Energy Radiation

Exposure of hydrocarbon polymer molecules to high-energy radiation results either in a decrease in their molecular weight or intermolecular interaction, with the eventual formation of an insoluble network. The primary factor which determines what happens is the relative incidence of fracture of the main chain of carbon atoms to cross-link formation. The ratio of fractures to cross-links, β, has usually been estimated from studies of the solubility of irradiated polymers. The bulk of such work has been on polyethylenes, and even under comparable experimental conditions widely differing estimates of β have been reported. Measurements of the stress relaxation during irradiation have also been used in an attempt to obtain alternative estimates of the chain fracture during irradiation[1].

One of us has recently developed an analysis which permits the calculation of both degree of cross-linking and the molecular weight of primary molecular chains cross-linked into the network from simple extension stress–strain measurements[2]. This analysis requires the determination of two elastic constants C_1 and λ^*; the value of C_1 depends upon both the frequency of cross-links and the molecular weight of primary molecular chains, while the value of λ^* depends solely on the former.

These three methods have been used to study the fracture of purified natural rubber exposed *in vacuo* to a 4-MeV. electron beam. No quantitative analysis of the solubility data was attempted as it did not conform to the behaviour predicted by Charlesby and Pinner from theoretical considerations[3]. However, the results indicated that there was little consummated chain fracture as the sol fraction tended to less than 0·7 per cent after long periods of irradiation. Approximate values of β of 0·14 and 0·11 were obtained from stress–relaxation and stress–strain measurements respectively. The value of β obtained from stress–strain measurements may prove to be an under-estimate, as it is based on a calibration involving the assumption that no chain fracture occurred in the formation of networks by the thermal decomposition of di-*tert*. butyl peroxide.

An approximate calculation in which it was assumed that: (1) all bonds in polyisoprene have an equal probability of fracture and (2) the fracture of each carbon–hydrogen bond results in the formation of one cross-link gave a value of β of about 0·5. It thus appears probable that chain fracture followed by direct recombination was a frequent reaction. Such a reaction would escape detection by any of the three methods of analysis, although the stress–relaxation method should detect the combination of the ends of fractured chains into the network[4].

These three methods of analysis are now being used to investigate both the effect of additives and the temperature of irradiation on the value of β, and experimental data will be published in the near future.

Samples were irradiated at Wantage Radiation Laboratories (Atomic Energy Research Establishment), and we thank Dr. R. Roberts and members of the Technological Irradiation Group for their kind co-operation.

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Etch Pits on Calcite Cleavage Faces

IN a recent communication, Watts[1] describes a number of etch pits found in freshly cleaved calcite, and in particular notes that three, four- and five-sided pits are found, with the first two types having some curved sides. I have also observed similar shapes, and have examined these under a surface-finish interference microscope (C. Baker of Holborn, Ltd.) using a × 40 objective and a mercury vapour lamp with a green filter ($\lambda = 0 \cdot 564\mu$). This type of interferometer compares the surface under investigation with a reference surface in the objective, and shows a magnified image of the surface crossed by fringes. These fringes are straight for a perfectly plane surface, whereas irregularities cause the fringes to be shifted into a pattern that may be likened to a contour map, of vertical spacing $0 \cdot 273\mu$. The number and direction of the fringes in the field may be varied by tilting the specimen.

All the investigations were on calcite plates that had been freshly polished to a high optical standard parallel to a cleavage plane, or parallel to the optical axis. These plates were first examined by various interferometric and optical transmission methods, and only those plates selected for the investigation in which no internal optical irregularities of any kind could be detected.

The surfaces were etched with 10 per cent hydrochloric acid for 10–60 sec., and then washed in distilled water.

Fig. 1*a* shows a cluster of four-sided etch pits in a surface parallel to a cleavage plane. The typical concave nature of the walls is clearly shown by the form of the fringes. A similar etch pit is shown in Fig. 1*b*, but with a single isolated pit in one wall of approximately an eighth of a micron deep. Fig. 1*c* shows a line of overlapping five-sided pits. Several lines of fringe disturbances appear to originate from the vicinity of the pits. It is possible that the line of pits may be due to preferential etching along a dislocation line.

The remaining photographs are of etch pits obtained on surfaces of plates cut parallel to the optical axis of the crystal. In this case, the pits are boat-shaped, as shown in Fig. 1*d*. With longer etching, the ends become more rounded (Fig. 1*e*), but the pits never appear to become circular. If the microscope stage and the specimen are tilted, the fringes can be made to cross a pit, as in Fig. 1*f*, to show its typical rounded bottom.

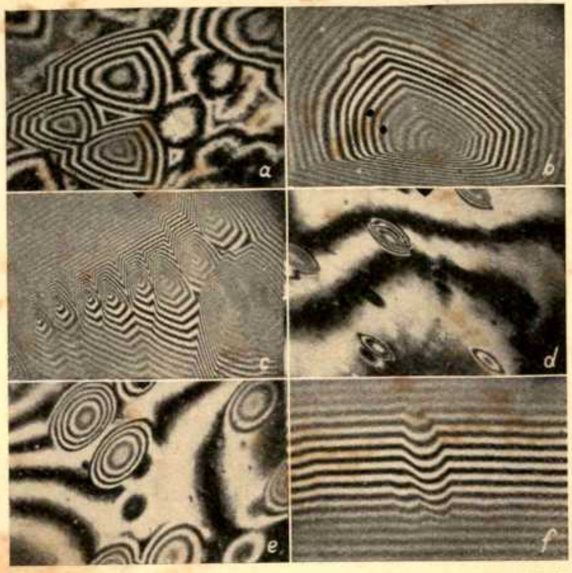

Fig. 1. (*a*) Four-sided etch pits, 20 sec. etching; (*b*) four-sided etch pits, 20 sec. etching, showing isolated hole in curved wall; (*c*) line of overlapping pits, 60 sec. etching; (*d*) boat-shaped etch pits, 10 sec. etching; (*e*) boat-shaped etch pits becoming rounded after 30-sec. etching; (*f*) rounded bottom of boat-shaped etch pit, 10-sec. etching. (× *c*. 40)

It is most noticeable, in these interferograms, how precipitous is the edge of a pit; there appears to be no rounding of the fringes at an edge.

I am indebted to the directors of C. Baker, Ltd., at whose works these photographs were obtained.

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Origin of Libyan Desert Silica-Glass

SINCE first reading of Libyan Desert glass[1], I have been intrigued concerning its origin. In the course of investigation of impurities in the glassy state, the role of trace germanium in fused silica was studied[2,3]. All fused silica produced artificially from natural quartz contains trace germanium impurity. Two different fused silicas investigated contained 0·9 p.p.m. of germanium[3]. It occurred to me that the trace germanium content of Libyan Desert glass might offer a clue to its origin, as no trace germanium would be expected to volatilize selectively (as germanium(II) oxide) during sudden melting and quenching of a high silica-content glass.

Table 1 gives the results of trace analyses of germanium, using a modified method of Schneider and Sandell[4], in Libyan Desert silica-glass, Libyan Desert sandstone, a Libyan Desert quartzite, two Libyan Desert sands, Aouelloul crater 'impactite' glass, two obsidians, the average for tektites from eleven different localities, including all known sources except Billiton (Darwin glass and americanites excluded), and the range for the non-magnetic portions of six meteoritic stones. It is seen that the Libyan Desert silica-glass contains very nearly the same germanium content as Libyan Desert sands. The average germanium content of the four materials from the Libyan Desert (other than glass) is 0·77 p.p.m. This agrees very closely with the value 0·80 for the Libyan Desert silica-glass and is not too different from the value for impact glass from the

Table 1. Spectrophotometric Analyses of Trace Germanium in Silicates

Silicate	Source	Ge content (p.p.m.)
Libyan Desert silica-glass	25° 2′–26° 13′ N. 25° 24′–25° 55′ E.	0·80
Libyan Desert sandstone	Gebel Qatrani District, north El Fayum, approx. 29° N. 31° E.	0·52
Libyan Desert quartzite	Gebel Qatrani district, north El Fayum, approx. 29° N. 31° E.	0·95
Libyan Desert sand	Gebel Qatrani District north El Fayum, approx. 29° N. 31° E.	0·77
Libyan Desert sand	From dune 50 km. north of Ghat, Libya, approx. 25° N. 10° E.	0·85
Aouelloul Crater glass Impactite	20° 15′ N. 12° 41′ W.	0·64
Obsidian	Lipari, Ægean Sea	1·67
Obsidian	Iceland	1·68
Average for tektites from eleven localities		0·23 ± 0·13
Range of non-magnetic portion of six meteoritic stones		0·09 – 3·02

Aouelloul crater. Obsidian, in general, has about twice the germanium content of the Libyan glass. Tektites, with which Libyan Desert silica-glass is sometimes classified, all have lower germanium contents than the latter. However, stony meteorites bracket the value of 0·80.

In Table 2 an analysis of the Libyan glass is compared with that of Aouelloul glass and sandstone, as well as an Ivory Coast tektite. It is seen that its trace elements match the sandstone more closely than even the impact glass and is quite different from the tektite. According to the results of Friedman[6], the Libyan Desert glass contains an order of magnitude higher water than any tektite and three times as much water as the Aouelloul glass. The latter difference may be correlated with the higher silica content of the Libyan glass.

The dark areas in Libyan Desert silica-glass were found by absorption spectral measurements to be due to streaks of ferrous iron. The inhomogeneity, the presence of crystallites, and the streakiness of the ferrous-containing regions indicate that the glass remained molten for only a short time.

I conclude from the chemical and mineralogical content that Libyan Desert silica-glass is terrestrial in origin, being formed from Libyan Desert materials, most likely by impact of some cosmic body. In this regard the area around 22° 18′ N. and 25° 30′ E., containing explosion craters (as well as volcanic evidence)[9], should be more thoroughly investigated. Ehmann and Kohman[10] indicate a cosmic origin for Libyan Desert silica-glass based on the apparent presence of aluminium-26 and beryllium-10. However, the level of activity of aluminium-26, for which the measurement was the more reliable, is lower than that in chondrites and in australite, and may be due to some other cause than free-space cosmic radiation.

Table 2. Analyses

Element (oxide)	Libyan Desert silica-glass*	Aouelloul: Sandstone‡	Aouelloul: Glass‡	Ivory Coast tektite§
SiO_2	98·20	95·30	86·10	76·56
TiO_2	0·23	0·55	0·60	0·60
Al_2O_3	0·70	1·85	5·05	11·54
Fe_2O_3	0·53	0·45	1·45	0·17
FeO	0·24	0·05	1·45	3·99
NiO	0·02	Nil	0·025	—
MnO	—	0·02	0·05	0·08
MgO	0·01	0·40	1·50	3·60
CaO	0·30	0·80	0·90	1·62
Na_2O	0·33	0·20	0·05	1·32
K_2O	0·02	0·10	2·05	0·82
H_2O	0·064†		0·02†	0·0047†

Analysts:
* M. H. Hey (ref. 5).
† Friedman, I. (ref. 6); value under Ivory Coast is average of 17 tektite analyses from various localities.
‡ Anal. Centre Technique d'analyse chimique, Paris (ref. 7).
§ Lacroix, A. (ref. 8).

A detailed report on the germanium contents of tektites and stony meteorites will be published elsewhere.

The germanium analyses were performed by Mr. John Anania of this laboratory. I wish to thank Prof. Truman P. Kohman of the Carnegie Institute of Technology for discussion of the cosmic-ray-induced radioactivities, for the samples of Libyan Desert materials, and for the obsidians investigated.

Alvin J. Cohen

Plate Glass Research Project,
Mellon Institute,
Pittsburgh, Pennsylvania.
March 23.

[1] Oakley, K. P., *Nature*, **170**, 447 (1952).
[2] Cohen, A. J., *Phys. Rev.*, **105**, 1151 (1957).
[3] Cohen, A. J., Fifth Inter. Congr. on Glass, Munich, July 1959 (to be published in *Glastechnische Berichte*).
[4] Schneider, jun., W., and Sandell, E. B., *Mikrochim. Acta*, **2**, 263 (1954).
[5] Spencer, L. J., *Mineral. Mag.*, **25**, 425 (1939).
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[8] Lacroix, A., *C.R. Acad. Sci., Paris*, **199**, 1539 (1934).
[9] Sandford, K. S., *Nature*, **131**, 46 (1933).
[10] Ehmann, W. D., and Kohman, T. P., *Geochim. et Cosmochim. Acta* **14**, 364 (1958).

Diurnal Lapse of Signals from *Sputnik III*

The radio signals from Satellite 1958 δ 2 have been observed consistently on close transits at Blaxland, near Sydney, in Australia, since shortly after its projection into orbit in May 1958. Until recently no definite failure of signal was observed, although the pulsed modulation code has at times been erratic.

Since early in March, however, there have been definite lapses of modulation. Systematic observation with equipment previously described[1] has established that the modulation is now present only when the satellite is actually in sunlight and ceases soon after it enters the Earth's shadow. This can lead to confusion in casual observations as the transmission may be detectable for only part of a transit. In a particular transit it may actually be received by an indirect propagation path when the satellite is approaching or receding, but not during the closest part of that transit when direct transmission would be expected.

An interesting feature is that, on very close transits, in the absence of the pulse modulation, a weak continuous-wave signal can still be detected with sufficient strength to record the Doppler shift. The rate of Doppler shift definitely establishes the signal as transmission from the satellite. It can thus be very useful for radio tracking in the absence of modulation. This continuous radiation is audible, and visible on the records, as a background when the modulation is present, as can be seen in the diagram in the communication mentioned. The reason for this background radiation would no doubt be apparent if we had a little information on the emitting equipment.

G. H. Munro

Radio Research Board Laboratory,
Electrical Engineering Department,
University of Sydney. April 28.

[1] Munro, G. H., and Heisler, L. H., *Nature*, **183**, 809 (1959).

FORTHCOMING EVENTS

(*Meeting marked with an asterisk * is open to the public*)

Tuesday, June 2

Bone and Tooth Society (at the Institute of Orthopædics, 234 Great Portland Street, London, W.1), at 2.55 p.m.—Annual General Meeting, followed by Scientific Papers.

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Prof. C. M. Robertson: "Animals in Ancient Greece".* (Fifth of six lectures on "Animals in Archæology". Further lecture on June 9.)

Wednesday, June 3

Royal Society of Arts (at John Adam Street, Adelphi, London, W.C.2), at 2.30 p.m.—Mr. D. Stafford-Clark: "The Contribution of Psychiatry to Modern Medicine".

Geological Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Dr. N. Rast and Mr. R. V. Beavon: "The Nomenclature and Diagnostic Characters of Ignimbrites, with reference to Snowdonia"; Dr. D. S. Weedon: "The Gars-bheinn Sill, Isle of Skye".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. C. F. Powell, F.R.S.: "The Origin of Particles of Great Energy in the Cosmic Radiation".

Thursday, June 4

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Prof. D. M. S. Watson, F.R.S.: "The Myotomes of Acanthodians"; Mr. G. R. Coope: "A Late Pleistocene Insect Fauna from Chelford, Cheshire".

Royal Anthropological Institute (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Mr. W. B. Fagg: "A Field Report on Yoruba Art".

Polarographic Society (at "The Duke of York", 8 Dering Street, London, W.1), at 7 p.m.—Informal Discussion Meeting on "Some Polarographic Problems Encountered in a Private Consulting Practice" introduced by Mr. F. Kenyon.

Chemical Society (at Burlington House, Piccadilly, London, W.1), at 7.30 p.m.—Scientific Papers.

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned.

Assistant Lecturer (with a science degree, with special qualifications and preferably postgraduate experience in entomology or helminthology) in Zoology—The Secretary, West of Scotland Agricultural College, 6 Blythswood Square, Glasgow, C.2 (June 5).

Laboratory Steward (over 21 years of age, with previous laboratory experience, and preferably experience in the preparation of biological materials and in photography) in the Department of Botany—The Registrar, University College, Singleton Park, Swansea (June 6).

Lecturer (with research experience in pure mathematics) in Mathematics—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (June 6).

Principal (with high academic qualifications and teaching and organizing experience in a university department, grammar school or technical college) of Croydon Technical College—Chief Education Officer, Education Office, Katharine Street, Croydon (June 6).

Senior Lecturer (with a degree in chemistry or pharmacy and a postgraduate qualification) in the Pharmacy Department, to direct research and to undertake a limited amount of postgraduate teaching—The Registrar, The Technical College, Sunderland, Co. Durham (June 6).

Research Fellow (with a Ph.D. degree or equivalent research experience in physical-organic chemistry or biochemistry) in the Chemistry Department, for an investigation of the mode of action of germicides—The Professor of Chemistry, The University, Hull (June 8).

Research Fellow (with a Ph.D. degree or equivalent research experience) in the Chemistry Department, for work on adsorption from the liquid phase by carbon adsorbents, in collaboration with Dr. J. J. Kipling—The Professor of Chemistry, The University, Hull (June 8).

Lecturer (graduate in either physics or engineering) in the Department of Physics, either to develop electronic instruments for application in nuclear physics or to undertake development work on the Department's synchro-cyclotron or other accelerating machines—The Registrar, The University, Liverpool (June 10).

Lecturer (with qualifications in genetics, preferably with emphasis on animal genetics) in Animal Genetics—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (June 10).

Senior Lecturer in the Department of Anatomy, to be primarily responsible for the organization and teaching of anatomy in courses for postgraduate students—The Secretary, The University, Edinburgh (June 10).

Junior Lecturer (preferably with medical qualifications) in Physiology—The Secretary, Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1 (June 12).

Lecturer in Mechanical Engineering—The Registrar, Queen Mary College (University of London), Mile End Road, London, E.1 (June 13).

Assistant Lecturer in Philosophy—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (June 15).

Lecturer or an Assistant Lecturer in the Department of Physics—The Deputy Registrar, The University, Birmingham 15 (June 16).

Geologist (with an honours degree in geology) at the New Zealand Oceanographic Institute of the Department of Scientific and Industrial Research, Wellington, for research in problems of marine geology and particularly those of sedimentation—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. No. B.11/21/8 and mentioning *Nature* (June 17).

Lecturer in Chemistry, a Lecturer in Geology, a Lecturer (with a good honours degree in electrical engineering or physics, and preferably research experience in solid-state electronics) in Electrical Engineering, a Lecturer in Mathematics, a Lecturer in Psychology, an Assistant in Physical or Inorganic Chemistry, and an Assistant in Biochemistry at Queen's College, Dundee—Joint Clerk to the University Court, The University, St. Andrews (June 17).

Assistant Lecturers in Botany (2), Chemistry, and Psychology—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1 (June 19).

Assistant Lecturer in Physics—The Registrar, The University, Manchester 13 (June 20).

Lecturer (preferably with a knowledge of the theory and practice of mechanisms and automatic controls) in the Postgraduate Department of Applied Mechanics—The Registrar, The University, Sheffield (June 20).

Demonstrator (Assistant Lecturer) in Physiology—The Registrar, The University, Leeds 2 (June 22).

Chair of Theoretical Physics in St. Salvator's College—Joint Clerk to the University Court, College Gate, St. Andrews (June 27).

Demonstrator in the Department of Organic Chemistry—The Registrar, The University, Leeds 2 (June 30).

Head of the Department of Pure and Applied Physics—The Registrar, Royal Technical College, Salford 5, Lancs (July 1).

Senior Lecturer for postgraduate teaching in the Department of Pathology—The Secretary, The University, Edinburgh (July 1).

Lecturer in Psychology at the University of Tasmania, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 6).

Senior Lecturer in Organic Chemistry at the University of Western Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (July 31).

Assistant Lecturer (with an honours degree and interested in research work) in the Biology Section of the School of Pharmacy—The Secretary-Treasurer, Royal College of Science and Technology, George Street, Glasgow.

Biometrician (graduate in mathematics with an interest in biology) in the Section of Statistics, for duties involving consultation and research on the design and analysis of experiments—The Secretary, National Institute for Research in Dairying (University of Reading), Shinfield, Reading, quoting Ref. 59/7.

Research Assistant (with a degree or diploma in agriculture or allied subjects with some interest in grassland), for work in connexion with grassland, with some lecturing duties—The Principal, Seale-Hayne Agricultural College, Newton Abbot, Devon.

Senior Geologist (preferably with a Ph.D. degree in geology and experienced in subsurface stratigraphy, and an interest in economic geology) in the Research Section of the Petroleum and Natural Gas Branch of the Department of Mineral Resources, Regina, Saskatchewan—The Agent-General for Saskatchewan, 19 Chester Mews, London, S.W.1.

Senior Physics Master—The Rector, Glasgow Academy, Glasgow, W.2.

REPORTS and other PUBLICATIONS

(*not included in the monthly Books Supplement*)

Great Britain and Ireland

British Insects: a Simplified Key to the Orders. By P. Skidmore. Pp. 20. (Manchester: Flatters and Garnett, Ltd., 1958.) 2*s*. 6*d*. [33

Agricultural Research Council: Soil Survey Research Board. Soil Survey of Great Britain—Report No. 10, 1957. Pp. iv+43. (London: H.M. Stationery Office, 1958.) 5*s*. net. [33

Field Studies Council. Annual Report, 1957–1958. Pp. 28+4 plates. (London: Field Studies Council, 1959.) [33

Imperial Forestry Institute, University of Oxford. Thirty-fourth Annual Report, 1957–58. Pp. 28. (Oxford Imperial Forestry Institute, The University, 1959.) [33

Research and Development at the Heston Laboratories of Atomic Power Constructions Limited. Pp. 10. (London: Atomic Power Constructions Limited, 1959.) [33

Ministry of Education. The Structure of the Public Library Service in England and Wales: Report of the Committee appointed by the Minister of Education in September 1957. Pp. iv+57. (Cmnd. 660.) (London: H.M. Stationery Office, 1959.) 3*s*. 6*d*. net. [43

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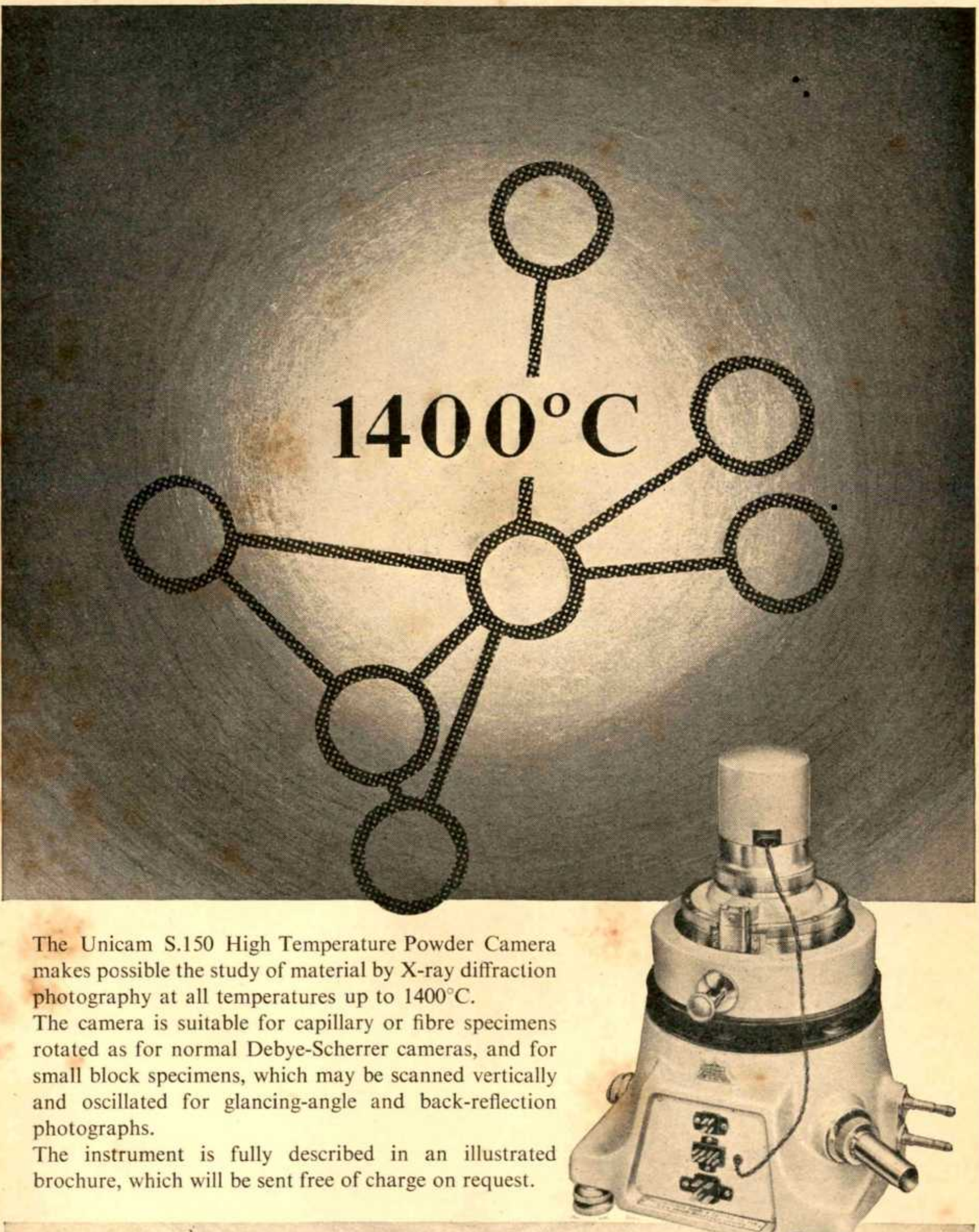

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ACADEMIC FREEDOM AND THE UNIVERSITIES OF SOUTH AFRICA

IT was taken for granted by the working party on higher education in East Africa, which recently formulated recommendations for the re-organization and extension of the Royal Technical College of East Africa, that it—as well as Makerere College and the University of East Africa, to be created eventually—would be multi-racial institutions as an indispensable element of their fully liberal nature and outlook. The University College of Rhodesia and Nyasaland has already been established as an inter-racial institution; although the two groups of students there live in different hostels, they mix without distinction in their academic work, in sport, and socially. This separation has indeed been challenged in Parliament in Great Britain, but the challenge brought not merely the desired reassurance but also evidence of a clear understanding of the nature of a university and deep respect for its autonomy.

These are vital factors if a young university institution is to establish conditions which will attract both Europeans and Africans, and enable them so to work together that the several races may make their full contribution to the development and welfare of the community. Already it is apparent that neither in Africa nor elsewhere is nationalism—or racialism—enough, and that if mankind is to gain control over events there must be the fullest possible contact of trained minds. The responsibilities which rest upon these young university institutions—and indirectly on the universities in Great Britain which have accepted special sponsoring relationships—are indeed heavy, and would tax all the experience of a mature university, with long and high traditions and an accepted place and wide influence in the community.

Even without the acute and inter-related problems of an adequate flow of students of high standard, sufficient well-trained teachers, facilities and opportunities for research, and appropriate relations with the community, including the support which professional associations are often able to give in Britain, it would not be easy for the university institutions which have developed overseas during the past fifteen years to meet the demands made on them for leadership. How much depends on the quality of leadership in the territories now achieving or verging on independence can scarcely be over-emphasized. But it is also true that the quality of the leaders forthcoming from the Colonial and overseas universities depends just as much as it does in Britain and the Dominions on the maintenance of the tradition of university autonomy, on the power of the universities to decide for themselves what students they shall admit, to select their own staff, to choose their fields of inquiry and to serve the community in such ways that their own experience and judgment indicate as best consonant with the work—in short on the tradition and ideals and the resources of a university.

The vital importance to-day of the contribution which the universities can make to leadership in society brings this question of academic freedom into the forefront. A university can only make its proper contribution to national life when it is assured of freedom to teach, to investigate, to discuss and to criticize. Deprived of any one of these, the quality of its intellectual life will decline, creative work may be stifled, research discouraged or discontinued, and ultimately the quality of its teaching sink to that of the school class-room. Amid the almost universal call for more scientists and technologists, for men and women capable of exercising responsibility and leadership in all walks of life, for handling with wisdom and vision the complex technical and human issues in an age of rapid technological change, and the unceasing discussion of how best such men and women can be found and trained, there is sometimes danger of the fundamental conditions which determine the quality of their training being overlooked.

Although there is impressive evidence from the past generation of the damage which is done to a country's real interests and to the character of its leadership by failure to respect the autonomy of its universities, the lesson does not appear as yet to have been fully learnt everywhere. That is a main reason why the whole academic world has followed with profound interest and concern the passage of the Separate University Education Bill, which on April 30 had its third reading in the South African House of Assembly. The Bill, which has been strenuously contested throughout by all the Opposition groups, has now only to go through the Senate before becoming law.

It is sufficient here to point out that the Bill provides for the creation of a series of colleges of higher education for the different Bantu peoples in South Africa, and separately for the Cape coloured people and Indians, but also prohibits the entry of non-white students to the present multi-racial universities of Cape Town and the Witwatersrand; it also removes from the University of Natal the powers it at present explicitly possesses of determining in what place a student is to receive instruction. The background was reviewed in *Nature* early in 1957 (179, 745; 1957), but since then the Committee on Science and Freedom has devoted two successive issues of its *Bulletin* to this question, the second of which (February 1958) reported very fully the impressive meeting on *apartheid* and the world's universities held in London in November 1957 (cf. *Nature*, 180, 1163; 1957). The Council of the University of the Witwatersrand also published papers relating to an interview regarding the Bill with the Minister of Education, Arts and Science in April 1957*.

These papers are still worthy of note for the dignity with which the Council of the University of the Witwatersrand affirms its opposition in principle to legislative enforcement of academic segregation on racial grounds, and deplores the interference of the Bill with the autonomy of the independent university institutions. Noting with deep regret the failure of the Government to consult any of the university institutions concerned in these matters, the Council affirms its conviction that although the university colleges for non-whites as proposed in the Bill may be able to provide instruction for the purposes of the examinations of the University of South Africa, these institutions cannot provide the equivalent of the university education which is available to non-whites at the open universities, and that the establishment of these institutions does not justify the Government in prohibiting the University of the Witwatersrand from continuing to accept non-white students. The provisions of the Bill are accordingly regarded as not merely repugnant to the tradition of universities, but also as specially repugnant to the South African university tradition, which does not admit the idea that the whole of a university staff should be subject to appointment by a Minister and that they should be controlled in all their university activities by Ministerial regulations and by a statutory code of discipline which stifles the academic conscience.

The meeting in London in November 1957 left no possible doubt as to the strong support which is forthcoming among the universities of the world for the South African universities in their protests against the Bill, or the extent to which their belief that the Bill will be grievously injurious to university education in South Africa; and their alarm as to the implications of the Bill are shared. In commenting on that meeting, however, *Science and Freedom* points out that, while Prof. L. J. du Plessis, of Potchefstroom University, gave convincing proof by his personal views and bearing that there are people in the Afrikaans-speaking universities of South Africa who sincerely believe that the development of the natives will best be fostered in their own segregated communities and in universities specially established to serve them on a tribal basis, he failed completely to convince the meeting that the Government of South Africa is equally sincere in this purpose, and that it is not primarily concerned to perpetuate the supremacy of the white race in South Africa. Concern as to possible effects if non-whites, by entering the universities and other cultural centres, should become competent to enter leading positions in the State continually frustrates positive elements in the Government policy; and there appears to be no room for consideration of the nature of a university and how it exerts its influence in society.

The openly expressed view of the Council of the University of the Witwatersrand that unless the Bill is withdrawn no independent university can in the future feel secure from Government interference with its academic freedom is further supported by the correspondence quoted in the papers referred to earlier. They record an attempt by the Minister of Education, Arts and Science to misrepresent in Parliament the University's attitude, which of itself would arouse grave suspicion as to the honesty of the Government's purpose. So far from attempting to explain to Parliament the nature of the university tradition and the dependence of the vitality of a university upon the freedom of teaching, of investigation, of discussion, and of administration that have long been accorded to such institutions in the civilized world, the Minister distorted what was said by the Chancellor of the University, and when challenged tried to gloss over the matter as of no significance. Nowhere in the long reply printed in these papers does the Minister show the slightest understanding of the argument put forward by the University, or of the extent to which its views as to the nature of a university and the conditions for its effective work are shared throughout the universities of the Commonwealth and the free world.

Nor are the authorities in universities of South Africa alone in protesting against the Bill. The National Union of South African Students has been no less active, and is convinced that the issues under test in South Africa are of more than local significance. It believes that the immunity of a university from State direction is one of the most necessary and valuable of our common heritages, the worth of which has been attested in many countries and many ages, and that the State should exercise its power to guarantee this right to a university and the right of all students to choose where they will be educated, not abuse it by enforcing conformity to its political doctrines.

An 'open letter' on the threat to the South African universities sent out by the National Union of South African Students in June 1958 explained clearly the doctrine of *apartheid* and the three measures (the other two are the Fort Hare University College Transfer Bill and the Durban Medical School Transfer Bill) which are designed to force this policy on the universities. The implications of these measures for academic freedom are indicated, and the letter points out that, although the Commission appointed at the last session of the South African Parliament to consider the details of the Separate University Education Bill was prevented from discussing the principle of the Bill, the evidence heard was almost unanimous in its condemnation of the main sections of the Bill. The letter admits, however, that it is unlikely that the Commission will make any recommendation which has not received the prior approval of the Cabinet; it was sent out in the hope of arousing interest, particularly from university men and women, but also from all who cherish the integrity of learning and the aspiration of youth to develop its talents freely and creatively.

* University of the Witwatersrand, Johannesburg. Papers relating to the interview between the University Council's Deputation and the Hon. the Minister of Education, Arts and Science on 1st April, 1957, on the matter of the Separate University Education Bill. Pp. 1+12. (Johannesburg: University of the Witwatersrand, 1957.)

Another message, from the International Committee on Science and Freedom, was published in the *Cape Times* and the *Cape Argus* on January 29, 1959. This Committee, which represents members of 296 universities in 52 countries, condemns in this statement the policy as striking at the roots of genuine university education and menacing the standing of South African universities as members of the world community of learning, and calls on the South African Government to take heed of the disastrous consequences of its policy and to abstain from its further pursuit. Both statements direct attention to the way in which the Government sees fit to ignore informed and responsible criticism, and the ill consequences to South Africa which may well follow if it comes to be regarded as a country which does not recognize the university autonomy common to the rest of the free world.

These newspaper comments show that the Government of South Africa, despite its denial of the opportunity of consultation to the universities, its refusal to meet and examine argument and the very dubious measures to which the Minister has stooped, has not been able to conceal the extent of the opposition to the Bill and the misgivings with which it is regarded. So late as April 16, a protest meeting was held in the Great Hall of the University of the Witwatersrand in Johannesburg, in which the principle at stake was once again emphatically affirmed: "We affirm in the name of the University of Witwatersrand that it is our duty to uphold the principle that a university is a place where men and women without regard to race and colour are welcome to join in the acquisition and advancement of knowledge and continue faithfully to defend this ideal against all who have sought by legislative enactment to curtail the autonomy of the university".

The meeting did not, however, limit itself to the reaffirmation of a principle: "Now therefore we dedicate ourselves to the maintenance of this ideal and to the restoration of the autonomy of our university". The affirmation is one required continually of every member of a university, be he a member of the academic or administrative staff, or student, and the service of the ideal of the free university calls for a like dedication. To the extent that it is publicly made in the universities of the Commonwealth, the members of the universities of South Africa should be encouraged, if not more tangibly supported, as they seek to fulfil their own hard task of restoring the autonomy of their universities. The goodwill in their task which is extended to them by their colleagues in the universities of the world will be reinforced by that of men and women everywhere who recognize that societies need centres of independent thought and criticism for survival, and the dependence of that function upon the guarantee of freedom and the free university. The future of mankind is so bound up with what is happening in Africa that it must still be hoped that the South African Government will reconsider its university policy, which must inevitably destroy its own powers of exercising the wise and humane and inspired leadership that is needed throughout Africa to-day.

EVOLUTION OF GENETIC SYSTEMS

Evolution of Genetic Systems

By Prof. C. D. Darlington. Second edition, revised and enlarged. Pp. x + 265. (Edinburgh and London: Oliver and Boyd, Ltd., 1958.) 21*s*. net.

More than a quarter of a century has passed since, as a young man, C. D. Darlington summarized and synthesized the then recent advances in (nuclear) cytology. The last chapter in this early book (1932) was entitled "The Evolution of Genetic Systems". It dealt with the origin of chromosomes and mitosis, the sexual cycle and meiosis, the spindle mechanisms, the cytology of differentiation, the stabilization of hybridity in apomixis, complex heterozygotes, and polyploids. Seven years later the chapter had grown into a small volume, published separately, in which the author "attempted to show genetics as the study of systems of heredity and variation which rest on the basis of the chromosomes and are related to one another by processes of natural selection". This book belonged to that famous group of evolutionary treatises by Fisher, Haldane, and Dobzhansky which integrated twentieth-century genetics with nineteenth-century evolutionary thought. It assigned to chromosomal cytology, as studied at the level of the light microscope, its place in evolution. This was a brilliant contribution of fundamental significance.

Once more twenty years have passed, and Prof. Darlington offers us a second edition of his work. He feels that genetics, while grown beyond many expectations, "does not seem to have grown beyond the framework I tried to give it". Many of the chapters of the new edition, therefore, are largely unchanged from their original form, although some additions and deletions everywhere show that this is more than a reprint. But there are also new chapters. One, on "The Management of the Cell", introduces all too briefly cytological aspects of development and differentiation such as the chemical hierarchy of deoxyribonucleic acid, ribonucleic acid and protein, and interrelations between nucleus and cytoplasm. Two other new chapters, near the end of the book, are entitled "Types of Plasmagene", and "Heredity and Infection". They "admit a third begetter" of genetics, Pasteur, "whose ideas on microbes and molecules", with those of Darwin and Mendel, "are becoming clearly imprinted on our diagram of nature". In these sections, Darlington discusses our knowledge of extra-nuclear transmission in *Drosophila*, *Culex*, witches' brooms, rogues in peas and tomatoes, and in other cases, and tries to unify it with modern insights into viruses, microbial genetics, and cancer. In a final new chapter on "Initiative in Evolution", the author compares what he calls "the general opinion of Darwinian geneticists" with his own conclusion from the analysis of the evolution of genetic systems. To the others he ascribes the view that natural selection can only produce results which are of immediate utility to the species, while he himself stresses the principle of pre-adaptation in which species acquire an infinite variety of mechanisms which are of no immediate use to them but prepare them for unexpected events. "An automatic property of foresight" is the ingenious label which he applies to this concept.

It cannot be expected that a revision of a book which had an important impact in the 'thirties will do the same in the 'fifties. The earliest insights have long become part of our thinking, either as possessions or as starting points for different views. The newer opinions on plasmagenes, infection, and differentiation seem less unique and more ephemeral. In details, one wonders why a wool-thread model of crossing over is still discussed and only a mention of molecular models of deoxyribonucleic acid and their relation to crossing over, why chromosomes are unreservedly called "molecules of immense size", why there is nowhere a treatment of the recent work on nuclear transplantation and differentiation, why the special X-chromosome–autosome balance in *Drosophila* is made to appear as a general scheme of sex determination, why "the virus" is called "a protein molecule", and why the references to the literature include so many minor items when some of the major ones are omitted. But we should not demand painstaking accuracy and coverage from an author whose merit has been to give us stimulating, if subjective, treatments of the place of cytology in genetics and evolution.

CURT STERN

NEW LIGHT ON OLD DARKNESS

Listening in the Dark

The Acoustic Orientation of Bats and Men. By Prof. Donald R. Griffin. Pp. xviii+413+16 plates. (New Haven, Conn.: Yale University Press; London: Oxford University Press, 1958.) 60*s*. net.

IN 1946, when zoologists everywhere were disentangling themselves from war-service jobs and trying to catch up with six years of unread literature, the most exciting discovery was Galambos and Griffin (1941) on "Obstacle Avoidance by Flying Bats". This short paper, though it raised more questions than it answered, carried instant conviction. Here evidently was the solution in principle of a problem which had rankled for 150 years. It only remained to determine in detail how the echo-location system of bats worked with the necessary sensitivity and precision.

This enchanting and enthralling book tells of the events leading to that epoch-making paper in 1941, and of the subsequent eighteen-year effort to answer the questions which it raised. But it tells much more. Dr. Griffin is no narrow specialist. He is that rare combination, a first-class experimenter who is also a first-class naturalist. A lesson implicit throughout the book—and a lesson that zoologists disregard at their peril—is of the degree to which the successful solution of a problem is dependent on the correlation of laboratory experiment with close and well-directed observation in the field.

The book opens with two chapters on the general biology of bats, including sections on their economic and medical importance and on migration and homing. Then there is an account of the genesis of the echo-location problem from Spallanzani's first observation in 1793 that bats, unlike owls, could avoid obstacles in complete darkness and Jurine's demonstration in the following year that this capacity was lost if their ears were blocked, to the suggestion of Hartridge in 1923 that bats emit high-frequency sound which generates a detectable echo.

There follow chapters on the voices of bats and on their hearing, on critical tests of their ability to avoid obstacles, and on the evidence of their catching insects by echo-location. So far the account is based principally on the Vespertilionidæ, which Dr. Griffin has known best and longest. Chapters 8 and 9 deal with echo-location in the long-eared bats, the horse-shoes, the fish-eating bats, the fruit bats and the vampires.

The remaining chapters carry the implications of echo-location beyond the Cheiroptera. There is an account of Dr. Griffin's own demonstration of echo-location by *Steatornis*, the oil-bird of Caripe, and of Schevill's evidence for echo-location by whales. There are instructive comparisons with the navigational devices of electric fish described by Lissmann and with the British inventions of Asdic and R.D.F. (now called sonar and radar respectively in deference partly to American susceptibilities and partly perhaps to euphony). There is a chapter with implications of serious practical importance on echo-location by the blind. Finally, Chapter 15, entitled "The Experimental Naturalist in Modern Science", is a persuasive and beautifully written plea for the preservation of an open mind, a plea which every zoologist should read with self-critical attention.

Although Dr. Griffin freely acknowledges the assistance he has received from physicists, it is clear that he has on occasion been hampered by their *obiter dicta* about what is possible and what is not, as Darwin was hampered by Kelvin's confident and erroneous assertions about the age of the Earth and the time available for evolution. *A propos* the possibility that *Noctilio* echo-locates fish just below a water surface (p. 244), "one physicist has told me that if I should persist in even considering it seriously he would cease to believe anything I ever have to say about bats and their acoustic orientation!" Dr. Griffin was more moved than he need have been by this horrific threat, which must have been based on prejudice and a failure to consider the conditions. A fish possessed of an air-bladder and situated half a wave-length below the surface will 'look like' a hole in that surface to an echo-location system situated above it: and the detection of such a hole would surely not offer any special problem to animals which can find a crevice in a solid wall or avoid a wire 0·25 mm. in diameter.

The index and bibliography seem to be both adequate and accurate. The book is well produced and misprints are very few. The text is also accurate wherever I have been able to check it, though I take exception to the statement on p. 146: "Under favorable conditions experienced human subjects can estimate the angular position of a sound source with an error slightly less than 10°". Under favourable conditions even inexperienced human subjects can do a great deal better than that: and so can cats and dogs and chickens, as Englemann showed long ago.

There is one inconvenient omission. Dr. Griffin, after thirty years of intimacy with bats, has altogether too much confidence in the non-cheiropterist's ability to assimilate and retain the systematic information in the first chapter of the book. There is nowhere to be found a table of bat affinity; and many readers may feel compelled, as I did, to make for themselves one showing the orders and families of bats and the position therein of each genus mentioned in the text, and its geographical distribution. It is to be hoped that future editions will include such a table in a form which allows quick reference.

On its factual content this book is well worth its place (and its not inconsiderable price) on any reference shelf, but content does not fully explain why, once begun, it is so difficult to put down until it is finished. Its grip is only partly due to the fact that it is written in vigorous, grammatical and intelligible English. On reflexion it seems to me that its charm lies in the candour with which Dr. Griffin recalls his expectations at every stage in his long pilgrimage, even when they led him astray, and the frankness with which he records the difficulties, practical and theoretical, administrative and financial, real and imaginary which he has encountered. Because he does not mind admitting his mistakes, one comes to realize that they have been extremely few. But the reader is carried expectantly and more or less effortlessly from crisis to crisis. The virtues of the authoritative treatise have been seamlessly welded to the virtues of the 'Whodunit', and the book can be recommended with confidence not only to the zoologist who must have it, but also to anyone at all with an I.Q. of more than 100 who can afford to buy it or who can beg, borrow or steal it. R. J. PUMPHREY

COSMIC-RAY SHOWERS

Extensive Air Showers

By Dr. William Galbraith. Pp. xvi+211. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1958.) 40*s*.; 7.50 dollars.

DR. GALBRAITH'S book on the extensive air showers of the cosmic radiation is a welcome addition to the rather limited number of books which deal with cosmic-ray phenomena. The author, in his preface, states that it is primarily intended for physics students and graduates who wish to find out what has been done in this field of research, and it may also find a more general appeal to workers in other realms of physics. It may be said at once that the book is ideally suited for a research student embarking on a study of some aspect of the cosmic radiation or nuclear physics, but I fear it is to be doubted whether those not directly interested in this limited field will be prepared for the concentration which is needed when reading this book.

In his introduction, the author gives an excellent résumé of the crucial experiments performed since extensive air showers were discovered in 1938 and the development of the theoretical concepts associated with them. The main body of the book contains eight chapters. The first chapter is mainly theoretical and deals with the photon-electron cascade in detail and the nucleon cascade rather more briefly, with a note on the problem of fluctuations. Five further chapters contain accounts of experiments, with the necessary theory interposed, and deal with the lateral density distribution of electrons, the penetrating particles, the density spectrum, longitudinal development and variations in the rates of extensive air showers. The two remaining chapters deal with experiments performed underground and the Čerenkov light produced by air-shower particles.

The impression that is left on reading this book is that here is a subject of such inherent complexity that there has been a definite tendency to set up apparatus and record results, rather than perform planned experiments with definite objectives in view. As a result the subject abounds with experimental results many of which are difficult to analyse in a way which furthers our understanding of extensive air showers. Dr. Galbraith's book will therefore be of the greatest use to future experimenters as he is not only a keen judge of an experiment from a practical point of view but is also able to see whether it leads to a better understanding of the subject. For this reason, Chapters 2–5, which at first sight may seem to be no more than catalogues of experiments, will repay careful reading. In the chapter on the Čerenkov effect we find traces of the enthusiasm for this fascinating subject which led Dr. Galbraith to participate with such success in the early experiments in which Čerenkov light was found to be associated with extensive air showers.

I should have preferred a fuller account of the statistical nature of the arrival of shower particles with a discussion of the Poisson distribution early in the book. The notation used where the Poisson distribution is discussed on p. 98 tends to be confusing, as the symbol m is used for the number of particles crossing a detector while m is used as an abbreviation for metre and in one case the italic m occurs as an unfortunate misprint. In general, the text of the book is very well set out and misprints are rare. Many of the diagrams, however, are small and confusing and some contain information which is not referred to in the text or contain symbols which do not agree with those of the text.

R. M. TENNENT

ADVANCES IN VETERINARY SCIENCE

Advances in Veterinary Science

Vol. 4. Edited by C. A. Brandly and E. L. Jungherr. Pp. xi+414. (New York: Academic Press, Inc.; London: Academic Books, Ltd., 1958.) 12 dollars.

THIS volume is composed of ten sections each dealing with problems of practical importance to the stock owner and the veterinary surgeon.

Of these sections, the second, which brings us up to date with information on radiation injury, and the eighth, which presents the current picture of the toxicity of insecticides and herbicides to livestock, will be more avidly scrutinized. At a time when civilization itself may seem to be at the mercy of radiation, the very full information and generous bibliography afforded by this volume are of real assistance to all whose duty it may be to plan and organize civil defence schemes.

As the authors wisely observe—"the widest port of entry into human beings of fission products is through animal products, particularly milk", and the role of veterinary science in maintaining a safe food supply in the face of radiation hazards becomes increasingly obvious.

The entry into the field of agricultural and veterinary parasitology of new insecticides, including the chlorinated hydrocarbons and the organic phosphorus compounds, has posed many problems. Knowledge in this new field is necessarily limited, but the chapter on this subject, if short, is none the less valuable and well supported by its references.

Chapters on defence against imported animal diseases, X-ray therapy in veterinary medicine, genetics and disease, and the epizootiology of leptospirosis bring further knowledge to that already marshalled in current veterinary literature and serve to emphasize once again the basis of a rational approach to these subjects.

Infectious diseases of sheep occupy an important chapter in which bacterial, rickettsial, viral and protozoal diseases of both lambs and adults receive full consideration.

Pigs have two chapters devoted to them—one on infectious atrophic rhinitis and one on enzootic virus pneumonia, and Glasser's disease. In view of the somewhat confused state of knowledge and understanding of these diseases, the clarity with which these chapters are written will be highly appreciated by all readers.

The chapter on Jöhne's disease is of paramount importance to British readers; with the anticipated eradication of bovine tuberculosis from Great Britain within the next few years, the problem of Jöhne's disease assumes new prominence. Indeed, it may well be that Jöhne's disease may be the next target of the animal health authorities in Great Britain. The problem of diagnosis of this disease is apparently far from solved, but, piece by piece, evidence on modes of infection is building a picture from a study of which must one day come a rational means of control and maybe eradication.

The contributors to this volume all deserve the highest praise for the quality of their essays; unnecessary diction is in all cases reduced to a minimum and references are unstintingly given.

If illustrations are somewhat regrettably few in number, the reader will appreciate the difficulties involved in copious illustration of the particular subjects covered. The verdict on this recent work must surely be that it appears at a time when the information it gives is urgently needed and that its readers acknowledge with gratitude the magnificent effort made by its distinguished contributors.

H. BURROW

CONTROL FUNDAMENTALS

Handbook of Automation, Computation, and Control

Edited by Eugene M. Grabbe, Simon Ramo and Dean E. Wooldridge. Vol. 1: Control Fundamentals. Pp. xx+1006. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 136*s.* net.

THIS is the first of a series of three volumes and is prepared by a staff of 29 contributors from an impressive cross-section of American universities and industrial organizations.

A handbook is expected to contain a body of material which is related by a common theme. The theme of this work is "Control Fundamentals", but this term has clearly been given a more general meaning than is currently ascribed to it in Britain. Only about half the volume is concerned directly with closed-loop control systems and their analysis and synthesis. The rest is devoted to general mathematics, numerical analysis, operations research and information theory.

The principle followed in Section *A* on general mathematics is to present the notation and major ideas and theorems of each subject chosen for treatment. For rigorous proofs the reader is referred to the generous bibliographies at the end of each chapter. The presentation is necessarily concise and applications of the various techniques described are not given. This leads to the obvious danger that the material may be regarded as insufficiently rigorous by the mathematician and insufficiently practical by the control engineer.

Three chapters in Section *A* are devoted to set theory, matrix theory, and Boolean algebra, respectively. Eight chapters are concerned with algebraic, integral, finite difference and differential equations, complex variable theory, conformal mapping, operational methods and Laplace transforms. Finally, two chapters deal with probability theory and statistics, respectively.

Section *B* on numerical analysis is likely to be of increasing interest as the use of digital computers becomes more widespread. Here are described interpolation and curve fitting methods, numerical differentiation and integration, matrix inversion, eigenvalues and eigenvectors and methods of solving differential and partial differential equations. Computer storage requirements and number of operations are given in tabular form for the various techniques.

Section *C* on operations research occupies 129 pages and is a fairly complete description of the methods used in obtaining optimum solutions to problems arising in industrial systems. It forms a useful introduction to the subject for the control engineer.

Information theory and transmission, in Section *D*, occupies 114 pages and contains a full exposition of the main concepts of information theory, prediction, data coding and the design of optimum filters. Useful curves and tables are given for the design of Butterworth–Thomson filters.

Feedback control in Section *E* occupies 427 pages. Here are presented the well-established techniques for the analysis and synthesis of control systems, with many valuable tables and curves. The first two chapters on methodology and fundamentals include tables of typical component equations and lists of analogous elements of electrical, mechanical and hydraulic form together with their transfer functions. The chapter on stability deals exhaustively with the use of the various graphical methods for stability determination. Transient and frequency response determination is described by analytical numerical and graphical methods. Design charts are given for deriving closed-loop transient and frequency responses from open-loop characteristics and a four-place table of sin x/x is provided for use with a numerical method of transient response determination. Feedback system compensation by series and feedback methods is described and tables are provided showing electrical, mechanical, hydraulic and pneumatic compensating networks and their transfer functions.

The chapter on noise deals with its mathematical description and measurement and with the response of linear systems to noisy inputs. Optimum design for stationary random inputs is treated.

In the penultimate chapter methods of non-linear system analysis are described with particular emphasis on the describing function method. Tables of describing functions are given for a large number of amplitude-dependent non-linearities. A surprising omission is the subject of noise in non-linear systems, on which much work has been published in the past few years.

Sampled data systems are rather briefly treated in the last chapter but useful tables are given of output transforms for basic sampled systems.

This handbook, in addition to presenting most of the existing techniques used by control engineers, also presents the mathematical framework on which much future development will depend. It will appeal most to research workers and development engineers in the ever-widening field of automatic control.

P. H. HAMMOND

Transistor Technology

Vol. 3. Edited by F. J. Biondi. (The Bell Telephone Laboratories Series.) Pp. xiii+416. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1958.) 94*s*.

DOUBTS were cast in the review of Vol. 1 and 2 of "Transistor Technology"—a review (see *Nature* of January 10, p. 72) written before the third and final volume was available—of the likelihood of the three volumes satisfactorily filling a serious gap left in the coverage of text-books and reference books. The doubts are largely dispelled by Vol. 3, however. It is only little more than half the size of either of the two earlier volumes, but it contains by far the best descriptions yet given of most of the modern techniques for making junctions and triode structures—many of them brilliantly conceived, carefully worked out and adaptable to large-scale production. It should appeal as strongly to newcomers seeking more than a superficial understanding of the techniques as to the more experienced research workers, technologists and teachers (though as yet this part of the subject is apparently little taught).

The book opens with chapters which classify the methods used to control impurity distributions and to form junctions in germanium and silicon, and show how the several ideas based on liquid-phase freezing and on diffusion in the solid can be exploited. The processes which monocrystalline semiconductors undergo in becoming diodes or transistors are next described. Some chemical processes and the making of ohmic contacts apply widely; others are more specialized, for example, jet etching, alloying and diffusion, the last two being treated in the detail warranted by their importance to-day. The last quarter of the book is on other branches of the subject. Some of the methods for measuring the rate of recombination of minority carriers, both in the bulk semiconductor and at the surface, are described; and a basis for designing equipment to measure selected parameters of transistors is analysed, in terms of ease, accuracy and value to the user. A few pages are devoted to reliability, a subject which is gaining importance.

The presentation of all three volumes conforms with the high standard of the series. It is to be hoped that we can look forward to further volumes, at intervals of a few years, keeping us up to date on material preparation and on device design, fabrication and performance.

J. R. TILLMAN

Studies in the Mathematical Theory of Inventory and Production

By Kenneth J. Arrow, Samuel Karlin and Herbert Scarf. (Stanford Mathematical Studies in the Social Sciences, No. 1.) Pp. x+340. (Stanford, Calif.: Stanford University Press; London: Oxford University Press, 1958.) 70*s*. net.

THIS book consists of a series of interrelated research papers. The results have been obtained during the past three years and are now published as the first volume of the new series of Stanford Mathematical Studies in the Social Sciences. Most of the research was carried out at Stanford University, largely under the auspices of the Office of Naval Research.

The quantitative study of inventory and production is a relatively new branch of applied mathematics; hence about the first fifty pages of the book are taken up with the historical background, the nature and structure of inventory problems, and summaries of the results of succeeding chapters. It is essential for the reader to study this part of the book, in order to grasp the general mathematical concepts which are developed later in special contexts. Part 2 consists of four papers covering the determination of optimal policies in the case of deterministic processes. One relates to production with marginal cost increasing with time, another to production planning with no storage facilities, and a third is concerned with the smoothing of production. Part 3 relates to stochastic processes and includes several papers on various aspects of the Arrow – Harris – Marschak dynamic model, and a paper relating to a hydroelectric model. The last part of the book is concerned not with the determination of optimal policies but with the operating characteristics of given 'simple' policies, and this is realistic in cases where it is impossible or too difficult to determine the optimal policy. There is a very important and interesting chapter on the application of renewal theory, including recent results of L. Takács.

It is only fair for the reviewer to point out that the present work involves advanced mathematics in every paper, and it is not likely to be understood by either managers or operational research workers who have only taken mathematics as a subsidiary subject at a university. It is certain that results of practical significance are implicit at various points throughout the book. But a good deal of sifting and simplification are necessary before the operational research man can find a result which he can take away and use at once.

L. S. GODDARD

Looking and Finding

By Geoffrey Grigson. Pp. 120. (London: Phoenix House, Ltd., 1958.) 9*s*. 6*d*. net.

ALTHOUGH well known as a writer on poetry, art, history and archæology, this is Geoffrey Grigson's first book for young people. The subtitle describes it as a help to "looking and finding and collecting and reading and investigating and much else". This breathless approach is continued throughout the whole of the not extensive text in which young people are advised how to start with maps and charts; how to use books and read them in "skipping and picking and jumping"; how to make discoveries about the houses they live in and what this has to do with inscriptions and phoenixes and salamanders; about yew trees and green men in churchyards; how boys and girls can make maps of their own manors with the fields, mills and ponds, and how to find, in the country, pack-bridges, toll-houses, tithe barns, wells, springs, withy beds, canals and locks, lime-kilns and many footpaths. In addition, young people are advised where to make archæological and palæontological discoveries and how to make use of museums. For those who wish there are also hints about how to make and manage their own art galleries.

Mr. Grigson's object in writing a book of this sort is wholly admirable, and parts of it will appeal considerably to some extraordinary children with somewhat unusual parents. The majority will find its pace too rapid, its frequent change of direction too violent, and its repeated exhortation to go and do something not so inviting as those sections where the author takes time off to show them what they should look for.

T. H. HAWKINS

MICROSEISMIC RESEARCH AT THE NATIONAL INSTITUTE OF OCEANOGRAPHY

By Dr. H. M. IYER and B. J. HINDE

GREAT BRITAIN is a good place for detailed research on microseisms, because the large number of storms with varying speeds and intensity that form in the Atlantic Ocean each year are usually well charted, and wave information is also available. Three important contributions which appear more or less as milestones in the history of the subject have been made from the British side. These are: (*a*) the wave-interference theory of microseism generation[1]; (*b*) the correlation technique for the estimation of composition and direction of propagation of microseisms[2]; (*c*) the design of the electronic-feedback seismograph[3].

Iyer[4], working on seismograph records from Kew Observatory, made a detailed analysis of microseisms associated with a number of Atlantic storms. The direction of approach of the waves at the recording station was estimated using a modified form of Darbyshire's correlation technique. The following were some of the results.

In general, there exists a composite microseismic source in the wake of a moving storm. The microseisms consist of a mixture of Rayleigh and Love waves. The Rayleigh waves form the main part of the information and the Love waves resemble background noise. The ratio of Rayleigh to Love waves resembles the usually accepted signal-to-noise ratio in any similar phenomenon, and appears to be a function of the distance of the generating source. Thus the farther microseisms travel, the smaller this ratio.

In the winter of 1957–58 nearly twenty major 'microseismic storms' were recorded by an experimental east–west component seismograph at the National Institute of Oceanography. Nothing more than visual reading of the records was possible from these single-component data, and the aim has been to have a three-component microseismic station equipped with a rapid data-handling system.

The new microseismic station has now been installed at the National Institute of Oceanography, Wormley, Surrey. It has two sections, the seismographs and the automatic analyser.

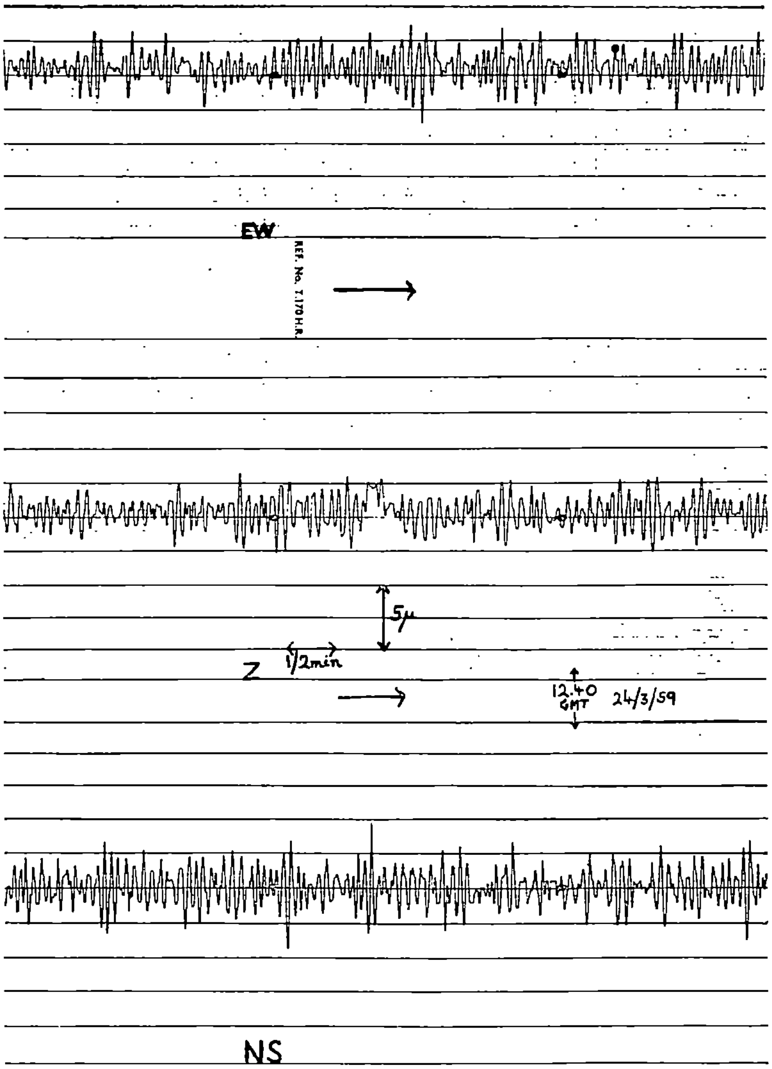

Fig. 1. Sample microseism record taken at the three-component microseismic station of the National Institute of Oceanography

The electronic feedback seismographs developed by Tucker[3] are used at the station. The seismograph has a very high magnification (up to 18,000) and a flat response from 1 to 10 seconds period, a combination of characteristics rarely obtained, though essential for microseismic research. The instrument is mechanically robust and easy to calibrate. In the properly engineered model both east–west and north–south components are incorporated in the same instrument, thus reducing the overall size of the station. The aim is to have a self-levelling system for the seismograph so that it can be buried in a borehole, thus eliminating the need for elaborate and costly seismograph vaults. A vertical-component seismograph employing the same principle has also been designed and is in operation. The instruments

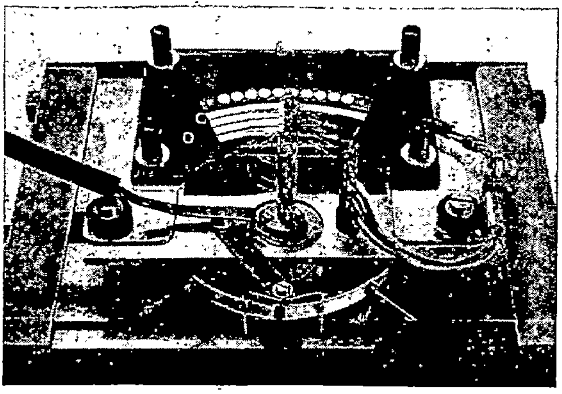

Fig. 2. The contact galvanometer used for directly analysing microseisms from seismographs

are at present accommodated in a brick-lined pit in the lawn, and the proximity of buildings, trees and the railway does not have any spurious effects. The electronics associated with the seismographs and the recorders are kept in the main building and are connected to the pit by cables. Fig. 1 shows a sample record taken on the three-channel recorder.

The information needed from the seismograph signals is root mean square amplitude, period, and the correlation coefficients between the components (for computing composition and direction of propagation). These computations must be made as the information comes through from the seismographs without any appreciable time delay.

The output from each seismograph is fed to a robust moving-coil meter provided with a system of platinized contacts (Fig. 2). The 'dot' or circular contacts are used for measuring root mean square amplitude and the 'strip' contacts for period and correlation measurements.

It is not proposed to explain here the detailed operation of the analyser. It will only be mentioned that the correlation coefficients are calculated by using the meters in two different channels to indicate automatically at regular intervals of time whether the arms are deflected in the same direction or opposite directions. This method has been used with great success by Akamatu[5] and Aki[6] in Japan for the study of short-period microseisms, in conjunction with an electronic computer for the analysis.

Fig. 3 shows schematically the final layout of the microseismic station. The filters can be set to study microseisms of different periods, and this as well as the complete sampling programme is controlled by the time-control circuit. The phase-shift network is used to correct for the phase difference between the horizontal and vertical components of Rayleigh waves in microseisms. For storage of information an automatic camera photographs the counters at the beginning and end of each operation.

Apart from the interest in microseismic study, such a seismic station should be of considerable interest to earthquake seismologists. A three-channel recorder has been provided for continuous recording for the benefit of those interested. The high magnification in the 1 to 10-second region should be of particular interest in earthquake studies.

Fig. 4 shows a sample record of an earthquake (epicentre 71° N., 8° E.) taken on the new seismographs (the three channels were recorded independently and put together). A very interesting pattern of long waves (75 seconds period) was recorded by the experimental east–west component seismograph on

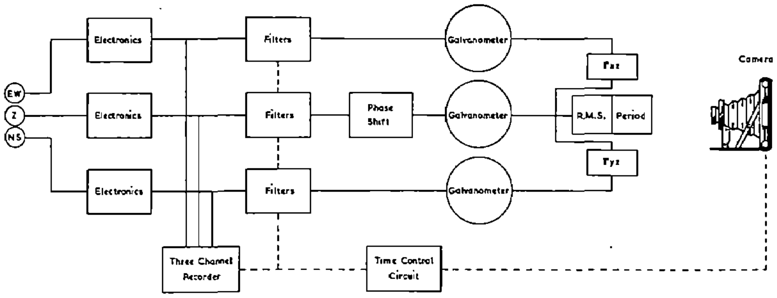

Fig. 3. Schematic diagram of a proposed microseismograph station

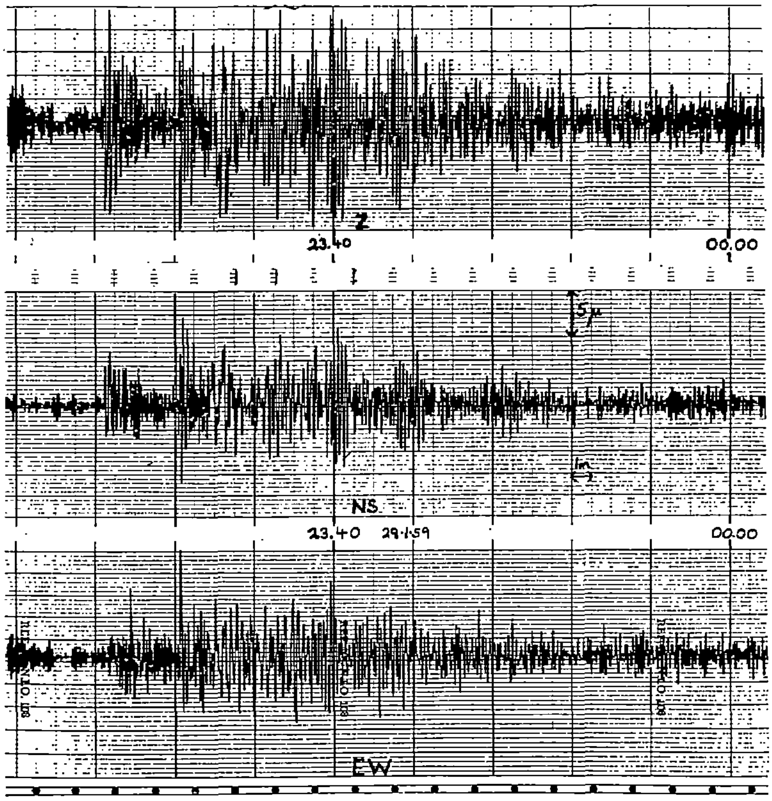

Fig. 4. A sample earthquake record (epicentre 71° N., 8° E.)

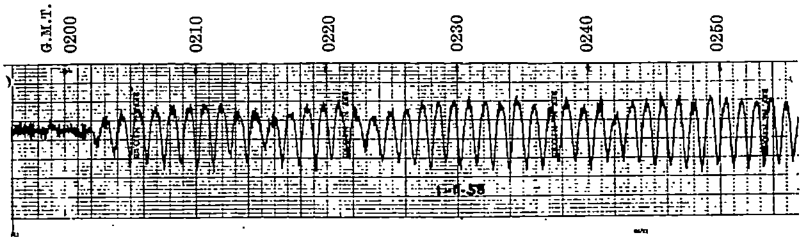

Fig. 5. A peculiar long-period record obtained on the east–west experimental seismograph between 0200 h. and 0250 h. G.M.T. on November 1, 1958

November 1, 1958 (Fig. 5). This could not be attributed to any earthquakes listed in the U.S.C.G.S. epicentre cards.

The system described might form the basis of a simplified storm-warning system in areas where such warnings are still needed. Vast expanses of the Pacific and Indian Oceans are inadequately covered meteorologically, and microseismic stations would be of great value in such areas. It is too early to predict the full utility of the new microseismic station from this point of view, but at least it can be said that it is a simple system with a sound theoretical and practical basis.

[1] Longuet-Higgins, M. S., *Phil. Trans. Roy. Soc.*, A, **243**, 1 (1950).
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INITIATION OF THERMAL REACTIONS BY THE FLASH ILLUMINATION OF ABSORBING BODIES

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MINUTE particles, filaments and foils of materials which absorb light have been heated to temperatures as high as several thousand degrees by absorption of a single intense flash of visible light. Heating by flash illumination may be used as a general technique for initiating thermal reactions rapidly, and in comparatively large volumes. The requirements are a high luminous flux falling on an absorbing body immersed in a transparent insulating medium. Using a variety of matrices and absorbers, many thermal processes, such as explosions, pyrolyses and phase changes, have been initiated within the few milliseconds of duration of the flash.

Heating by absorption of continuously emitted visible light has been used for many years[1]. Although Eggert[2] has used intense flashes of light to ignite explosives and oxidize thin aluminium foils, little has been reported on the dependence of thermal effects on the shapes and dimensions of absorbers or the nature of the matrix surrounding them.

Heating by flash illumination of heterogeneous systems first occurred in these Laboratories when samples of commercial polymers were placed, as shown in Fig. 1, along the axis of a spiral quartz discharge lamp (similar to lamp III described by Christie and Porter[3]) and flashed, using 5,000 J. from capacitors charged to 4,000 V. The heterogeneous pyrolysis of the polymers took place around normally occurring particulate impurities, yielding gases, carbon and fluorescent products[4]. Fig. 2 shows polyethylene sheet which had been placed in a borosilicate glass tube and degraded by exposure to one flash. The degradation is essentially independent of the chemical nature of the polymer, since polytetrafluoroethylene, regenerated cellulose, nylon,

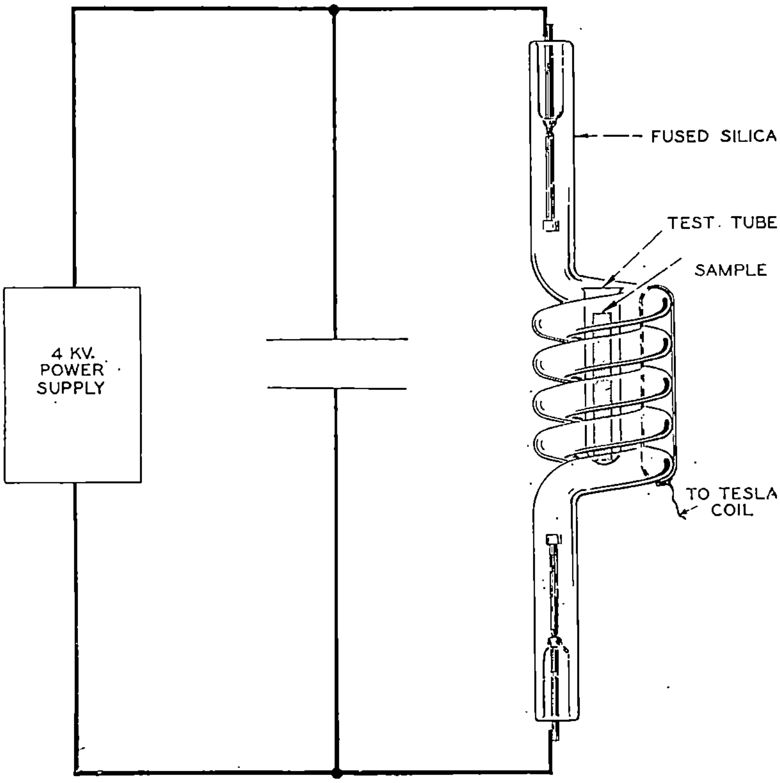

Fig. 1. Experimental arrangement for heterogeneous flash heating

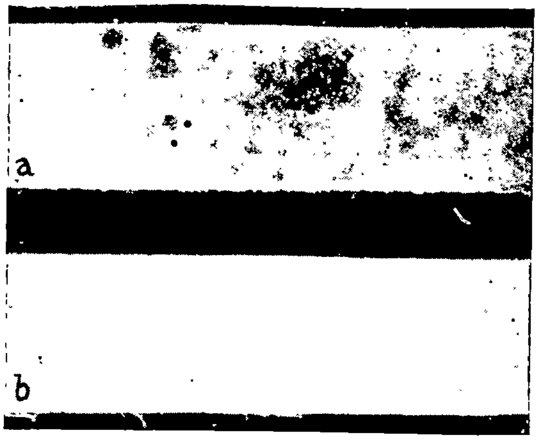

Fig. 2. (*a*) Polyethylene degraded by one flash of 5,000 joules at 4,000 V. (*b*) Control sample

polyethylene, polystyrene and poly*iso*butylene all behave similarly, unless carefully prepared without trapped particulate matter. Clean polymers do not show this type of decomposition in the flash, but can be degraded if absorbing bodies are suspended in them.

If an isolated absorber of small dimensions is irradiated in a transparent matrix, the rise in surface temperature can be estimated from simple heat-balance equations[5]. Fig. 3 shows temperature rises estimated in this way for graphite spheres, cylinders and plates of various radii or thicknesses suspended *in vacuo* or in a liquid hydrocarbon and flashed at half our maximum energy (648 μF., 4 kV., 2·5 msec.). As the radius r of the heated body decreases from large values (1,000μ) the temperature increases, because gradually less energy is used to heat the absorbing body by inward conduction. *In vacuo*, where no outward conduction into the matrix can occur, the surface temperature continues to increase as r decreases until the limit of black-body re-radiation of the incident energy is reached—for these flash conditions at about 4,100° C. for bodies of radius less than 1μ. The validity of this estimate was demonstrated by vaporizing *in vacuo* tungsten and molybdenum as well as carbon of these dimensions almost explosively in a single flash.

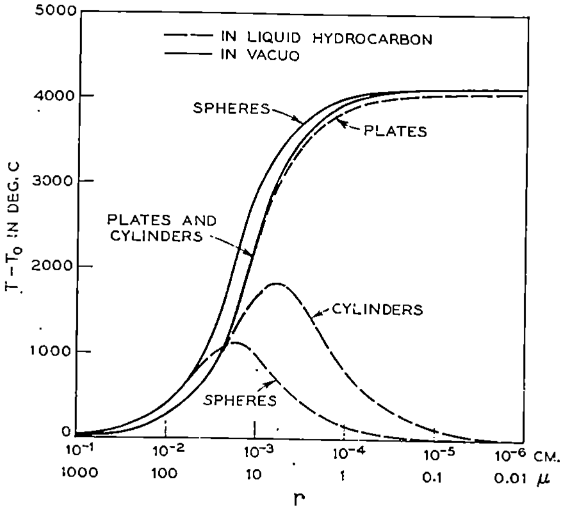

Fig. 3. Rises in temperature estimated for graphite-like absorbing bodies of various sizes exposed to flashes of 2·5 msec., 5,000 joules, 4,000 V.

When spherical or cylindrical absorbers are placed in a condensed transparent matrix such as a liquid or polymeric hydrocarbon, conduction of heat away from the absorbing surface occurs, and the surface temperatures decrease after going through maxima near 10μ. Thus, carbon particles of large diameter (1,000μ) and also carbon black of very small particle size (very much less than 1μ) do not initiate degradation in polyethylene, whereas particles in the size-range 1–100μ cause severe decomposition of the type shown in Fig. 2.

Absorbing foils or platelets, however, should achieve essentially similar surface temperatures in the flash, whether *in vacuo* or in a condensed medium, because heat conduction outward from a foil is not a function of thickness, compared with the strong dependence on radius in the case of spheres or cylinders. Thus, the highest maximum temperatures in condensed matrices should occur with absorbing foils less than 10μ thick.

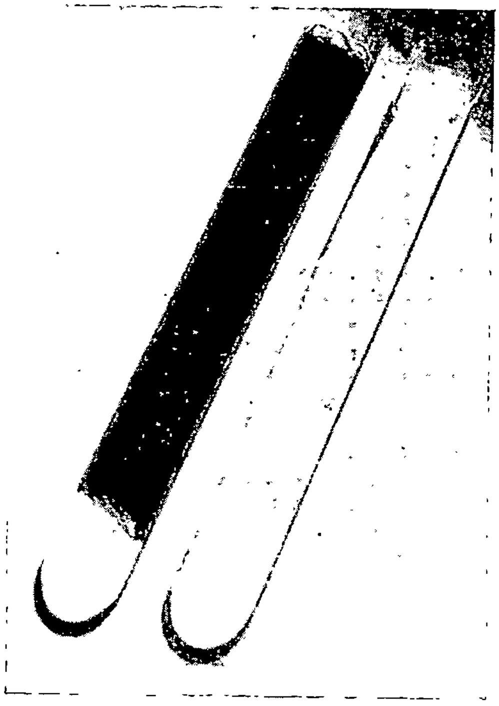

Fig. 4. Mineral oil flashed once at 10,000 joules at 4,000 V. Opaque sample contained 25 metres of 7·5-micron tungsten wire before flashing. Clear sample had no heterogeneous absorber

Because of experimental difficulties, we have never measured temperatures directly, but our experiments seem to be quite well explained by these estimates.

Higher maximum temperatures can probably be obtained by increasing the light intensity either by increasing the energy input to the lamp, or better, by decreasing the duration of the flash. Certainly, the temperature-range of ordinary chemical interest (up to 10,000° C.) seems readily achievable in heating times of 100 microsec. or less by flash heating with relatively modest energy inputs (of the order of 10^4 J.).

Heating by flash illumination has been used[5] to evaporate *in vacuo* powdered silver, carbon, chromium, molybdenum, nickel, tungsten and zinc of particle diameters less than 100μ. When flashed at fairly low intensities, metal foils 5–10μ thick were etched, revealing microstructure of the metal. At higher intensities the foil melted into a small droplet, and at still higher intensities vaporized[6]. Powdered coal has been vaporized and pyrolysed by flashing *in vacuo* and in hydrogen and halogen atmospheres[6].

Flash heating has been used to pyrolyse methane in the presence of 7·5μ tungsten wire; hydrogen, ethane, ethylene, acetylene and carbon were formed[6]. Explosions have been initiated in the systems methane–oxygen and hydrogen–oxygen by flashing these gas mixtures in the presence of borosilicate glass wool. While glass wool is certainly not a simple black-body absorber in triggering these explosions, nevertheless, the glass wool was heated to fusion temperatures[6].

Mineral oil has been flash pyrolysed using suspended molybdenum (less than 74μ) and carbon (less than 36μ) powders, glass wool (8μ) and tungsten wool (7·5μ) as absorbers. Flashing above a threshold energy caused the oil to become black with suspended carbon, effervesce, and fluoresce when excited by 3661-A. radiation. Fig. 4 shows two borosilicate glass tubes of mineral oil flashed once at 10,000 J. The tube with the opaque black suspension contained 25 metres of 7·5-μ tungsten wire, whereas the other had no absorbing material present before flashing. If the solids are filtered from the oil, an absorption spectrum is obtained which is similar to that of an oil degraded in service as a high-voltage insulator.

If a slurry of zinc dust in mineral oil or glycerine is flashed, the metal is evaporated and re-deposited in finer form but without degradation of the matrix. Zinc boils at 907° C.; thus, in the vaporization-redeposition process it must reach a temperature sufficient to pyrolyse the hydrocarbon. Upon flashing zinc dust suspended in polyethylene, zinc was evaporated, but no degradation of the polymer took place. It is possible that the quenching of free radicals by zinc vapour occurs, as in the Paneth mirror removal reaction[7].

Dark particles smaller than 90μ in diameter embedded in polymers become sufficiently hot to cause degradation when flashed above 10^3 J. Carbon, hydrogen, water, carbon monoxide, carbon dioxide, methane, acetylene, ethylene, ethane, and small amounts of higher hydrocarbons are produced when unclean polyethylene is flashed[4,8]. Since the carbon formed with one flash acts as an absorber during the next flash, the amount of degradation in polymers is cumulative with the number of flashes. Empirically, the total amount of gas formed from polyethylene is nearly proportional to the square of the number of flashes[8]. In addition, wax-like degradation products are expelled from the polymer during flashing, and fluorescent materials are deposited near the carbonized centres.

In gaseous or vacuum matrices, absorbing sheets or cylinders, such as wires, fibres or filaments, are the most convenient experimentally since they have known dimensions and shape, are self-supporting, and can be placed in known orientations in the system. Particulate absorbers may be suspended in liquid systems, but for careful work they always show the difficulties associated with agglomeration, poorly known shape, and a distribution of diameters. In very viscous liquids or polymers it is always difficult to incorporate materials without accompanying gas pockets or other disturbances, and reproducibility is never high. In most systems cylindrical absorbers are the most easily handled experimentally.

The experiments described here demonstrate the applicability of rapid heating by flash illumination of absorbers of small dimensions. Further, the similarity of the time-scale and experimental arrangements to the flash photolysis technique[9] suggests its use for preparing free radicals in systems which do not absorb light from the usual flash sources. The chemical effects are somewhat similar to those of shock waves but can be produced in liquid and solid systems as well as gases, to form much greater instantaneous volumes of reaction intermediates. In effect, heating by flash illumination is a heterogeneous sensitization which transfers optical energy from photons unable to cause discrete photochemical processes via thermal excitation into chemical energy, an over-all process quite analogous to true homogeneous sensitization. However, unlike flash photolysis with or without sensitizers, flash heating of absorbing bodies depends little on wave-length of the flash; it often has a threshold intensity below which no discernible reaction occurs, and it has present a hot reactive interface or, in more extreme cases, hot vapour from the absorber, to complicate the reaction.

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DARWINISM AND THE STUDY OF SOCIETY

TO mark the centenary of “The Origin of Species”, a conference was arranged at the instigation of the Scottish Branch of the British Sociological Association and held in Adam House, Chambers Street, Edinburgh, during April 8–10. Originally it was envisaged as something of an investigation into the origins and development of Social Darwinism. This intention underwent some change at the hands of the *ad hoc* organizing committee of natural and social scientists from Scottish universities, but the public purpose of the conference emerged as a discussion of the effect of the publication of “The Origin of Species” on social theorizing, and an examination of the present bearing of biology on sociology.

These two main themes became at times closely interwoven, and the core of the conference discussions was, in many ways, Prof. C. H. Waddington's paper on “The Human Evolutionary System”. This was nothing less than an attempt to fit Social Darwinism out in modern dress: to read human history and social development in the light of the biologist's interpretation of evolution.

Waddington began with a concise but extremely lucid exposition of the evolutionary system, under four headings: (1) exploitation, the 'choice' of a particular environmental niche out of the range of possibilities open to any creature, and the possible modification of that environment; (2) epigenesis, the complex and interacting processes by which the development of the fertilized egg into the mature organism is controlled, processes which possess resilience in surmounting obstruction or damage, tend towards the coherent organization of all the single parts, and seek pre-determined end-points of growth; (3) genesis, the transmission of separable hereditary characteristics actually or potentially present in the parents; (4) natural selection, the environmental factors which may favour, challenge, or destroy the possibilities of reproduction. This four-fold system applies, of course, to man as to other animals, but Waddington proposed that it might provide a theoretical model, or at least a number of interesting suggestions, for the interpretation of the evolutionary processes apparent in human history. If one sees the creation of the mature organism from the fertilized egg as a continuous series of chemical accretions and processes going on under controls established by the 'information' stored in chromosomes, then, at this level of abstraction, the theoretical system devised by biologists to account for evolutionary change might conceivably apply to the changes occurring in the more complex, but essentially similar, passage of information from generation to generation of men by a multiplicity of extra-genetic channels.

For example, the genetic make-up of a population tends to resist disturbances which might change it by natural selection; after such a disturbance is withdrawn, the frequencies of genes in the gene pool return towards their previous values. "Something near to this biological genetic homoeostasis in its strict sense . . . are the somewhat nebulous, but often easily recognizable, qualities which are often spoken of as national characteristics, such as Jewishness, or Indianness". Another specific analogy is suggested by the process of introgressive hybridization in plants, which results from the persistence or loss of whole chromosomes. When this happens, a whole "chunk of genetic information", more or less randomly associated, is passed over. The agglomerations of cultural items passed between social groups sometimes appear to be fortuitously associated in a similar way, like trousers with Western technology.

Mr. Maynard Smith's commentary, and the subsequent discussion, fastened on the empirical character of genetic transmission and mutation on one hand, and human history on the other, and not on the conceptual utility of Prof. Waddington's models. Prof. Waddington's picture of an epigenetic landscape formed into watersheds, gullies and valleys by developmental controls is presumably a crude heuristic representation of a very complex process about which, even yet, little is known; it is a way not so much of explaining facts as of keeping what is to be explained in mind. Seen in this light, there is probably something to be gained by a method-starved science like sociology from such broad sketches, taken not as a means of suggesting testable hypotheses but as illustrations of the conceptual strategy employed in a related, and more sophisticated, discipline. Mr. Maynard Smith, however, chose to attack this—and by implication, any other—attempt to work from biological to historical explanation. The material differences he cited are not in dispute: the sub-human evolutionary system works with little or no transference of characteristics acquired metagenetically, whereas there is continuous alteration of social institutions and culture by the interaction of individuals with each other, with their social inheritance, and with their physical environment.

In fact many, if not most, of the sociological analogies quoted in Waddington's paper are very dubious parallels to the genetic and epigenetic models brought into play. The resilience and durability of Jewishness can scarcely be equated with lack of adaptability; this is a familiar sociological instance of cultural adaptation to manifest or latent subordination, along with the well-defined characteristic speech and manners of Negroes in the southern States of the United States: and the association of trousers with steam-engines and trading posts is only non-functional in a very restricted technological sense.

Maynard Smith took the view that the Marxist interpretation was the best attempt so far made at a usable theory of history, its weakness lying not in any fundamental error in Marx's own approach but rather in the failure of his followers to treat his ideas critically or to modify them in the light of advances in other fields. He did not think that one could usefully start from evolutionary theory and then attempt to find historical analogies for the various entities and items involved. Prof. Waddington, he said, had failed to point to any process in history comparable to natural selection, the most important single concept in the theory of evolution.

I have little doubt that a quick glance through the record of patented inventions, or the history of revolutionary epochs in England, France and Russia, even a reading of "Doctor Zhivago", would reveal plenty of instances of natural selection at work in the field of technological or political innovation. The crux of the difficulty lies, as Dr. J. Bronowski hinted at the end, in our present incapacity to isolate a single 'billiard-ball' entity from which to build explanations of variation in human society, as biologists have done with the gene—the unitary member of a pool of available characteristics constantly replenished by mutation and reduced by natural selection.

For Bronowski, this represented a failure by sociologists to respond to the challenge of Darwin's work. It was a double challenge, and a double failure. The first was the implicit question in his work of how variation occurred, a question which the later science of genetics was developed in order to answer. The second was the introduction of the notion of chance into rational explanation. This had, he claimed, proved a necessary foundation for the future not only of biology but also of physics.

In reality, chance has figured very largely in the historian's rendering of his subject. It accounts partly for the outlawing of pattern, interpretation, and theory by historians, and becomes explicit, though disguised, in the remark of H. A. L. Fisher's, quoted with such approval by K. R. Popper: "Men . . . have discerned in history a plot, a rhythm, a predetermined pattern . . . I can see only one emergency following upon another . . . only one great fact with respect to which, since it is unique, there can be no generalisations". But historians have used chance as a flag of surrender rather than as a weapon, and students of society have been content to name tendencies rather than establish laws. Prof. Morris Ginsberg's paper, "Social Evolution", was itself an admirable demonstration of the classic procedures of sociologists, and of the very different manner in which they have developed the concept of evolution and met the questions it poses. It discussed at some length attempts by nineteenth-century and later social scientists to develop evolutionary interpretations of the course of development of language and technology, and less successfully, of religion and law. He then presented his own view of social evolution as a process of development through higher levels of organized complexity of rational ideas, this process being effected by the human capacity for the intercommunication of ideas and skills.

Prof. Lancelot Hogben, by contrast, made his contribution on "Darwinism and Human Society in Retrospect" an exercise in the interpretative view of history he has made his own—which one would like to call philotechnic commensalism: the fortuitous concurrence and subsequent interaction of circumstances, generating complex causal processes which determine the direction and the variations in the rate of cultural development in different sections of the human species. The technological backwardness of the African is thus related to the susceptibility of horses to trypanosomiasis, which "has condemned Africans south of the tropic of Cancer to be their own beasts of burden in territories where malaria, yellow fever, hook-worm infection, schistosomiasis and many other diseases only lately recognized by medical science exact a heavy toll from the vitality of the people". Furthermore, "every change of the human environment through human interference signalizes a new accretion of transmissible experience and a new potential of further change. Because of this, human society is a unique ecological system". Thus, Darwin's work fits logically into its historical position when seen in the context of the stage reached by technological developments available in England by the mid-nineteenth century; the most significant circumstances being the greater facilities for sea travel offered by steam power, which "both greatly enlarged opportunities for a global survey of living beings and forced the problems of geographical distribution on the attention of naturalists", the accumulation of evidence for evolutionary succession provided by the work of survey and excavation undertaken during the railway-building period, and the major improvements in the microscope. The formulation and reception of Darwin's contribution to evolutionary theory similarly falls into place among the controversies over the criteria which should determine admission to the universities, the Civil Service, commissioned rank in the army and other controllerships, the debate over free competition as a principle of economic welfare and a social ethic, and the re-sharpening of the Abolitionist conflict in the years before the outbreak of the American Civil War.

In turn, the grand theological debates of the next forty years appear now to be locked firmly within their ideological setting; and the fruitless search for a complete genealogy of organic creation, Hogben also suggested, is visible now as the inescapable fate of a biology unprovided with the means of distinguishing adequately between hereditary transmission and genetic variation.

While Hogben's and Waddington's contributions inevitably dominated the conference, as latter-day reflexions by Darwin's scientific successors on the possibilities and limitations of a biological view of human society, other topics bulked larger than this short notice can easily show. Prof. Basil Willey's introductory account of the descent of Darwin's own theories from previous writings, although stretching back to Empedocles, was subject to a good deal of emendation in later discussions; his restriction of the effect of his work to the theological debate was deplored, and his view of Darwin's ultimate religious position as "helping to restore buoyancy to religion by forcing it to abandon some of its more untenable defences" was rejected by both *rapporteurs*. His paper also, however, bore on Darwin's introduction of the notion of chance into the rational interpretation of universal destiny, ideas far more disruptive than Newtonian mechanics, which had made the retention of the notion of design and of Designer plausible.

Mr. S. A. Barnett, in the last session, returned to the attack on Prof. Waddington's side with a range of suggestions from the study of the behaviour of bees, rats, birds and fish which might throw some light on behaviour in infancy, on motivation or emotion, and on the nature of language and human communication in general. Mr. Tom Burns, in the final paper, regarded these suggestions as limited to a very small field of human conduct, which characteristically selected courses of action from the wide range of possibilities available as normative guides to members of any society.

At the close of this conference, Dr. Bronowski remarked that no title could have lent itself better to so diverse an array of papers on such different subjects. Survivors of conferences on cybernetics may dispute this, but a conference which began with observations on the "history of man's endless probings into the mystery of existence; his thoughts about the nature of reality, about the administration of the universe . . ." and ended with a muted discussion on chance as the mechanism of irreversibility, and thus as the instrument of the universal order apprehended by man, has some claim to catholicity. It was also, far more frequently than one expects any conference to be, absorbingly interesting and seminal.

The conference papers will be published in book form.

TOM BURNS

OBITUARIES

Dr. L. J. Spencer, C.B.E., F.R.S.

LEONARD JAMES SPENCER, who died on April 14 at the advanced age of eighty-eight, was fourth in a line of distinguished keepers of minerals in the British Museum. His predecessors were Story-Maskelyne, appointed the first keeper of the department a century ago, Sir Lazarus Fletcher and G. T. Prior. All three were Fellows of the Royal Society, to which Spencer also was elected in 1925. He was made C.B.E. in 1934, he was given the Murchison Medal of the Geological Society in 1937, and the Roebling Medal of the Mineralogical Society of America in 1941. He was an honorary member of the Mineralogical Societies of Germany and of America, a senior Fellow of the Geological Society of London, and was president of the Mineralogical Society during 1936–39, and its foreign secretary from 1949 until his death.

Spencer was born at Worcester on July 7, 1870, the eldest son of James Spencer, for many years headmaster of the Day School Department of Bradford Technical College. According to a note in a local paper on the occasion of his appointment to the British Museum, he was "nurtured on examinations" and "when he had just completed his seventh year he turned his serious attention to geology . . .". From Bradford he went with a Royal Exhibition to the Royal College of Science for Ireland, taking a first in chemistry. Thence with a scholarship he went to Sidney Sussex College, Cambridge. He won the Harkness Scholarship in 1893 and successfully competed for a vacancy in the Department of Mineralogy in the British Museum (Natural History) in the same year. He then went for six months to Munich to study under Paul Groth, using his Harkness Scholarship money for the purpose, and returning to take up his appointment at the Museum on January 1, 1894. He married in 1899 Edith Mary, daughter of Islip J. Close, of Mortimer, Berkshire, and leaves a son and two daughters.

Spencer's main achievement in the Department of Mineralogy, apart from his scientific research work, was the establishment of the system of registration, labelling and card-cataloguing the mineral collection. After Prior became keeper in 1909, Spencer did a great part of the registration himself, and one result of his work and of his careful training of those who followed him is that the National Collection of Minerals is now probably the best documented and indexed in the world.

In addition to all his meticulous work on the collection, Spencer's output of original papers was considerable. His publications number well over a hundred and range over a wide field of descriptive mineralogy. He published two books, on minerals and on precious stones, and he translated from the German two large quartos on the same subjects. He took up the study of meteorites after Prior's retirement in 1927 and contributed many papers on this subject to the *Mineralogical Magazine*.

The discovery of the meteorite craters at Henbury in Australia and Philby's discovery immediately afterwards of the crater at 'Wabar' with its slag-like masses of silica-glass black with included millions of tiny spheres of nickel-iron gave great impetus to Spencer's work in this field and led him also to take up the problem of the origin of tektites. He strongly advocated the theory that tektites are the product of the impact of great meteorites on the Earth's surface, a theory that still finds many supporters but remains unproved. It was his interest in these problems that led him at the age of sixty-four to accompany an expedition into the heart of the Libyan Desert to investigate on the spot the masses of yellow silica-glass discovered in 1932 by P. A. Clayton. He hoped to find a meteorite crater there, but returned with the problem of the origin of the glass still a mystery. Spencer retained a very active interest in meteorites right to the end of his life, and his very last publication on meteorites was a communication in *Nature* of March 8, 1958.

Spencer's work at the British Museum would have filled the working life of some men, but he seemed always to be doing the work of three. In 1901 he took over the editorship of the *Mineralogical Magazine* from Miers, and he continued to edit it until the end of 1955. Previous to 1901 he had catalogued mineralogical papers for the Royal Society Catalogue for 1883–1900, and he continued this for the International Catalogue of Scientific Literature for 1901–14. In 1920 the Mineralogical Society commenced publication of *Mineralogical Abstracts*, and Spencer edited it and prepared more than half the abstracts himself. When he retired he had edited twelve volumes covering thirty-six years. A dinner in his honour was given him by his friends in November 1950 on the completion of his fifty years as editor of the magazine, and he lived to see *Mineralogical Abstracts* appear in a new format as a joint British–American publication aiming at a still wider international coverage of the science.

W. Campbell Smith

Dr. Eric Berkeley Higgins

Dr. Eric Berkeley Higgins, who died suddenly on April 8 at the age of seventy-three, was an inventor of the classical industrialist type, which pioneered industrialism, and is still not quite extinct. He had the peculiar flair for chemical development which seems to combine art and science. After early success with Dr. Ormandy, he invented the use of nickel formate in the hydrogenation of oils, and found his capitalist in Hamburg, where he was busy getting the process started when the First World War broke out.

Higgins was arrested in November 1914, and became one of a large number of Englishmen collected, under very unpleasant conditions, from all over Germany. These finally arrived in the Ruhleben racing stables at Spandau, where most of them stayed for the duration of the War, under the supervision of neutral diplomats. The American ambassador soon condemned one barrack (twenty-four horse boxes with hayloft above) as unfit for human habitation, so this was handed over to the already very active representatives of the arts and sciences among the prisoners. The scientists included established research men in physics, chemistry and biology, one of whom eventually became a Nobel prizeman. Soon a laboratory for teaching and research in all these branches came into existence, and Higgins was one of its most active spirits. He had arrived at the camp with two young men just gazetted out of Woolwich, with a sound mathematical training but no science. Higgins made them both change to science as a career, and one of them received his knighthood for it.

The power which Higgins had to enthuse gifted youth, and gain their warm personal regard, played no small part in his subsequent success, which culminated in Catomance, Ltd., which he worked up from small beginnings on his inventions in waterproofing and mothproofing materials. When he showed the latter some years ago at a chemical exhibition in London, he directed attention to it by providing a few live moth grubs engaged in chewing wool, with a microphone and loudspeaker which made them audible to visitors. This naturally appealed to the B.B.C. reporter touring the exhibition, and all the world heard the nasty little fellows munching.

Higgins had a mind the energy of which seemed entirely undiminished by several spells of ill-health. He would be at it hammer and tongs, first at Liverpool making soap, then at Brentford on water-softening compounds and naphthol *AS* dyes, then at Welwyn Garden City on the intensive development work which brought prosperity. He enjoyed to the end the affection of the men and women who formed the firm which he created, and all his life-long friends.

H. Stafford Hatfield

TABLE OF ARTIFICIAL EARTH SATELLITES

From the Royal Aircraft Establishment, Farnborough, Hants. May 8, 1959

Name	Launch date, life-time and descent date	Shape and weight	Size	Date	Orbital inclination (deg.)	Orbital period (min.)	Perigee height (n. miles)	Apogee height (n. miles)	Orbital eccentricity	Argument of perigee (deg.)
**Sputnik* 1 1957α2 instrumented sphere	1957 Oct. 4·8 ? 92 days ?1958 Jan. 4	Sphere 184 lb.	23 in. dia.	1957 Oct. 4·9 1957 Oct. 25·8 1957 Dec. 25·1	65·1 65·1 65·0	96·2 95·4 91·0	122 120 110	513 471 254	0·052 0·047 0·020	58 49 23
**Sputnik* 1 1957α1 rocket	1957 Oct. 4·8 57 days 1957 Dec. 1	Cylinder? —	—	1957 Oct. 4·9 1957 Nov. 4·0 1957 Nov. 24·3	65·1 65·1 65·0	96·2 94·0 91·0	122 119 110	513 403 254	0·052 0·038 0·020	58 45 36
**Sputnik* 2 1957β	1957 Nov. 3·1 162·0 days 1958 Apr. 14·08	Payload 1,120 lb.	? 70 ft. long	1957 Nov. 4·00 1958 Jan. 4·00 1958 Feb. 21·00 1958 Mar. 25·00 1958 Apr. 9·00	65·33 65·29 65·26 65·23 65·21	103·760 100·505 97·105 93·785 90·780	122 119 114 107 97	902 739 570 402 253	0·0987 0·0802 0·0605 0·0400 0·0215	59 35 14 359 352
Explorer 1 1958α	1958 Feb. 1·16 4 years	Cylinder 30·8 lb.	80 in. long 6 in. dia.	1958 Feb. 1·16 1959 Jan. 3·05 1959 Mar. 21·06	33·2 33·2 33·1	114·8 111·7 111·2	191 189 189	1,379 1,228 1,203	0·141 0·125 0·122	121 139 296
Vanguard 1 1958β2 instrumented sphere	1958 Mar. 17·5 ? 100 years	Sphere 3¼ lb.	6·4 in. dia.	1958 Mar. 17·5 1959 Mar. 12·5	34·3 34·3	134·18 133·94	353 353	2,140 2,129	0·191 0·190	129 274
Vanguard 1 1958β1 rocket	1958 Mar. 17·5 ? 100 years	Cylinder 50 lb.	4 ft. long 20 in. dia.	1958 Mar. 17·5	34·3	134·18	353	2,140	0·191	129
**Explorer* 3 1958γ	1958 Mar. 26·73 93 days 1958 June 28	Cylinder 31 lb.	80 in. long 6 in. dia.	1958 Mar. 26·73 1958 May 15·0 1958 June 14·13	33·3 33·3 33·3	115·7 104·8 96·8	101 97 93	1,511 970 565	0·166 0·110 0·063	 326
Sputnik 3 1958δ2 instrumented cone	1958 May 15·3 19 months	Cone 2,926 lb.	12·3 ft. long 68 in. dia.	1958 May 15·3 1958 Nov. 17·00 1959 Mar. 2·9	65·19 65·16 65·13	105·97 103·000 100·750	122 120 118	1,015 867 754	0·111 0·095 0·082	58 351 310
**Sputnik* 3 1958δ1 rocket	1958 May 15·3 202·4 days 1958 Dec. 3·7	Cylinder? —	— —	1958 May 15·3 1958 Aug. 15·10 1958 Oct. 11·25 1958 Nov. 13·66 1958 Nov. 30·59	65·19 65·14 65·09 65·04 65·00	105·9 102·000 98·000 94·000 90·000	122 119 115 108 95	1,011 816 615 413 217	0·111 0·089 0·066 0·041 0·017	58 26 5 347 339
Explorer 4 1958ε	1958 July 26·63 13 months	Cylinder 38·5 lb.	80 in. long 6 in. dia.	1958 July 26·63 1958 Oct. 25·06 1959 Mar. 21·02	50·3 50·3 50·2	110·18 107·73 102·37	142 140 138	1,193 1,073 805	0·128 0·115 0·085	50 317 60
**Atlas* 1958ζ	1958 Dec. 18·96 33·6 days 1959 Jan. 21·6	Cylinder 8,700 lb.	80 ft. long 10 ft. dia.	1958 Dec. 18·96 1959 Jan. 1·78 1959 Jan. 17·02	32·4 32·4 32·3	101·47 98·12 92·67	104 95 88	796 627 355	0·089 0·070 0·037	130 249 37
Vanguard 2 1959α1 instrumented sphere	1959 Feb. 17·67 ? 50 years	Sphere 21·5 lb.	20 in. dia.	1959 Feb. 17·67	32·9	125·7	301	1,790	0·166	135
Vanguard 2 1959α2 rocket	1959 Feb. 17·67 ? 50 years	Cylinder 50 lb.	4 ft. long 20 in. dia.	1959 Feb. 17·67	32·9	130·0	302	1,992	0·184	135
**Discoverer* 2 1959γ	1959 Apr. 13·89 13 days 1959 Apr. 26·5?	1,300 lb.		1959 Apr. 13·9 1959 Apr. 24·6	90 90	90·4 88·9	130 103	190 132	0·008 0·004	160 96

NOTES: Dates are given in days and decimals of a day U.T. 1 nautical mile = 6,080 ft. = 1·853 km. Perigee and apogee heights for *Sputniks* are over an earth of radius 3,435 n.m. and for U.S. satellites over an earth of 3,442 n.m. Argument of perigee is the angle from northward crossing of the equator to perigee, measured along the orbit. The orbital values for the *Sputniks* are from British observations and theory. Those for the U.S. satellites have been compiled from a variety of sources. It is not known whether *Discoverer* 1, launched February 28, 1959, achieved orbit; it was, nevertheless, designated 1959β. * Indicates satellites no longer in orbit.

NEWS and VIEWS

International Meteorological Organization Prize, 1959: Prof. J. Bjerknes

THE Executive Committee of the World Meteorological Organization has this year awarded the annual prize, provided by funds left by the International Meteorological Organization on the formation of the World Meteorological Organization, to the eminent Norwegian meteorologist, Prof. J. Bjerknes, who is now professor of meteorology at the University of California, Los Angeles. Prof. Bjerknes is known to meteorologists everywhere for his work, in conjunction with his father, the late V. F. K. Bjerknes, T. Bergeron and H. Solberg, in the initiation forty years ago at Bergen of the technique of frontal and air-mass analysis in weather forecasting. With the same meteorologists as those noted above, he collaborated in the writing of a major text-book on dynamical meteorology, "Physikalische Hydrodynamik", published in 1933. Before the War he carried out much research into the structure of depressions, as revealed by the release of a large number of sounding balloons at frequent intervals from one place for a number of hours, and with the dynamics of convection in the atmosphere. Since the War he has been particularly concerned with research into the general circulation of the atmosphere. He was professor of meteorology at the Geophysical Institute in Bergen from 1919 until 1931 and went to Los Angeles in 1940. In international scientific work he has been both secretary and president of the Association of Meteorology of the International Union of Geodesy and Geophysics. British meteorologists, to whom he is well known as an honorary Fellow (1932) and Symons Gold Medallist (1940) of the Royal Meteorological Society, welcome this award to one of their most distinguished, genial and unassuming colleagues.

Chemistry in Relation to Medicine at Edinburgh: Prof. G. F. Marrian, F.R.S.

PROF. G. F. MARRIAN, who is to retire from the chair of chemistry in relation to medicine in the University of Edinburgh, moved from Toronto to Edinburgh in 1938 to succeed Prof. George Barger. He had already established his reputation by the isolation of pregnanediol in 1929, œstriol in 1930 and œstriol glucuronide in 1936. He gathered a group of workers and proceeded to isolate a considerable number of new products of steroid metabolism, notably 16α-hydroxyœstrone, and more recently he has also worked on the metabolism of adrenal cortical hormones. He developed new methods of estimation of steroids of clinical importance for diagnostic purposes. On his advice, the Medical Research Council set up a Clinical Endocrinological Research Unit at Edinburgh and he took a considerable part in its management and direction. Latterly he served on the Agricultural Research Council, the Medical Research Council and the Advisory Committee for Medical Research in Scotland.

With the institution of a six-year curriculum at Edinburgh in 1949, Marrian took over the teaching of biochemistry to medical students. For them his lectures provided an exceptionally clear and illuminating introduction to the subject. After a few years, the teaching of chemistry to medical students, which was previously the Department's main teaching duty, was handed over to the Department of Chemistry, so enabling the Department of Biochemistry to undertake the teaching of biochemistry to dental and to veterinary students and to strengthen the science courses in biochemistry, which now include a flourishing honours year.

Prof. R. B. Fisher

DR. R. B. FISHER, who is to succeed Prof. Marrian at Edinburgh, took the Final Honour School of Animal Physiology in the University of Oxford in 1929, became a departmental demonstrator immediately and a University demonstrator in due course. For more than twenty-five years he was one of the most sought-after teachers of biochemistry in Oxford. Undergraduates reading medicine learned from him a critical approach to the literature and an eye for nonsense which left a permanent stamp upon them. Colleagues in many biological departments made a habit of asking for his criticism and advice on their papers, on their design and statistics. He did the same useful service officially as an editor both on the *Journal of Physiology* and the *Biochemical Journal*. He was away from Oxford for some years during the Second World War, directing an Air Ministry Group concerned with the design and analysis of strategic bombing. He belongs to the select race of chemical physiologists, and prefers to work on unquestionably living cells. He has demonstrated creatine synthesis in the surviving heart, and is using the perfused heart for work on the effects of insulin on permeability. He devised a method of studying absorption in surviving small intestine and has written a book on "Protein Metabolism", which is widely known as a critical appraisal of accepted views.

Fisheries Research: Dr. H. A. Cole

DR. H. A. COLE, who took up his duties as director of fisheries research on May 1, in succession to Mr. R. S. Wimpenny (see *Nature*, 181, 159; 1958), joined the Ministry of Agriculture, Fisheries and Food as an assistant naturalist in 1933 when he was appointed to the Laboratory at Conway. During the period up to the war he was largely concerned with an examination of the development and setting behaviour of oysters in tanks and of the incidence of parasites. In the war he was seconded to the Yorkshire (West Riding) War Agricultural Executive Committee, serving as a deputy chief executive officer. When he returned to the Conway laboratory in 1946 he resumed and extended his interests in oyster culture in a manner which rapidly made him an outstanding authority in his field. Plans for the rehabilitation of oyster beds which arose from this work resulted in the establishment in 1953 of a new fishery laboratory at Burnham-on-Crouch largely devoted to this purpose. Dr. Cole succeeded the late Mr. R. E. Savage at this juncture as head of the Shellfish Section, with his headquarters at the new laboratory. From here he and his staff produced much valuable advice on the cleansing and rearing of shellfish and initiated a considerable amount of development work on culture and pest control. In addition to this Dr. Cole found it possible to foster a substantial amount of new research work. This included, besides the nanoplankton food of the larval oyster, investigations into the natural history and exploitability of cockles, clams, whelks, scallops, shrimps, crabs and lobsters. When the International Council for the Exploration of the Sea founded its Shellfish Committee Dr. Cole was appointed the English representative. For the past three years he has served as the chairman of this body, effecting a useful integration of the several national programmes and working successfully towards standardization of methods. In 1954 he was offered the Buckland Professorship, choosing for his series of lectures the title "Inshore Fisheries", and in February 1958 he was appointed deputy director of fisheries research.

Mr. R. J. H. Beverton

Mr. R. J. H. Beverton, who succeeds Dr. H. A. Cole as deputy director of fisheries research in the Ministry of Agriculture, Fisheries and Food, joined the Fisheries Laboratory, Lowestoft, as a scientific officer in 1945. Having taken a first in zoology in Part 2 of the Natural Sciences Tripos at Cambridge and the Frank Smart Prize as best student of the year, he devoted a good knowledge of mathematics and his sympathy for this subject to considering a mathematical formulation of fish stocks under the influence of fishing. Working in the Population Section under Mr. Michael Graham he quickly developed the subject, and in conjunction with Mr. S. J. Holt, now of the Food and Agriculture Organization, has produced a manual on the subject of population dynamics of fish species which is a classic and which has made him a world authority in this field. During the past ten years he has produced numerous papers and memoranda and his advice, offered directly or indirectly to international bodies such as the Permanent Commission of the 1946 Fisheries Convention, the International Council for the Exploration of the Sea, and the International Commission for the Northwest Atlantic Fisheries, has made his position as an adviser on fisheries conservation quite outstanding. In addition to this he has twice been called on to visit and report on the fisheries of the Colonial dependencies; in the first instance Lake Victoria Nyanza and in the second the sea fisheries of the Kenya and Tanganyika coasts. He has also been twice invited abroad to give a course of lectures on his subject, once in the United States and once in Canada. Mr. Beverton succeeded Mr. Michael Graham as head of the Population Section at Lowestoft when the latter retired in February last year. In addition to the very considerable volume of direct research work on which he is engaged, Mr. Beverton has been responsible for developing the collection of research statistics and fish measurements at the ports on a scale that has not been equalled elsewhere.

Kalinga Prize : Prof. Karl von Frisch

Prof. Karl von Frisch, of Munich, the eminent zoologist, well known for his research on the sensorial physiology of insects and fish, has been awarded the Kalinga Prize for popularization of science. The prize of £1,000 is offered annually by the Kalinga Foundation, which has been set up to contribute to the economic, social and cultural progress of the Indian State of Orissa. The purpose of the award, as stated by Mr. B. Patnaik, its donor, is to offer recognition to leading interpreters of science and also to strengthen links between India and scientists of all nations.

Space Research in Britain

Following the Prime Minister's statement on the British space research programme, in the House of Commons on May 12, the Lord President of the Council has appointed a Steering Group on Space Research, under the chairmanship of Sir Edward Bullard, with the following terms of reference: "Subject to the responsibility of the Lord President of the Council, in consultation with the other Ministers concerned, for the supervision of the Government's Space Research Programme, to advise on the formulation of that programme, and to co-ordinate the arrangements for its execution".

The membership of the Group is as follows: Sir Edward Bullard (*chairman*); Prof. W. V. D. Hodge, secretary of the Royal Society; Prof. H. S. W. Massey, University College, London; Sir Harry Melville, secretary, the Department of Scientific and Industrial Research; Sir Graham Sutton, director-general of the Meteorological Office; Dr. R. van der R. Woolley, Astronomer Royal; and senior officials representing other interested government departments. The Steering Group had its first meeting on May 27.

Space Monkeys

On May 28 two monkeys were recovered unhurt from the nose cone of an American Jupiter missile after a space-flight of 1,500 miles. The flight lasted about 15 min.; the missile reached an altitude of about 300 miles and attained speeds of up to 10,000 m.p.h. During the flight reports of the monkeys' heartbeats, muscular reactions, pulse, temperature and respiration were, among other things, relayed back to Earth. The animals seem to have been little affected by the violent acceleration and the 9-min. period of weightlessness which they experienced. They will probably appear on television. The nose cone also carried samples of yeast, corn, mustard seed and fruit-fly larvæ, and, in order to study the effect of weightlessness on the processes of fertilization, phials of the eggs and sperm of sea-urchins which were mixed when the missile attained its maximum velocity.

Department of Scientific and Industrial Research Committee on Metal Fatigue

A committee to review current research needs on the fatigue of engineering structures and to survey existing research facilities has been set up by the Council for Scientific and Industrial Research following an approach from the Institution of Civil Engineers. The committee will not include aircraft structures, reinforced concrete structures, or metal physics in the scope of its review, though information gained in these fields will be used. Sir Alfred Pugsley (University of Bristol) has been appointed chairman. The other members of the committee are: Sir Donald G. Bailey, Mr. T. Baldwin, Mr. H. L. Cox, Mr. O. A. Kerensky, Mr. H. M. Pemberton, Mr. C. E. Phillips, Prof. S. C. Redshaw, Dr. P. B. Walker and Dr. R. Weck. The committee's terms of reference are: "to review current research needs on fatigue of engineering structures (metal), to survey existing research facilities and to make recommendations to the Department of Scientific and Industrial Research". The committee is interested in examining records of failures or accidents which might have been due to structural fatigue, even if fatigue was not recognized as the initial cause. Such information may be helpful in revealing areas in which further research work is needed.

Regional Technical Information Services

In reply to a question in the House of Commons on May 12, Mr. H. Nicholls, Parliamentary Secretary to the Ministry of Works, as representing the Lord President of the Council, said that the Department of Scientific and Industrial Research was helping active local organizations to build up regional technical information services based on Birmingham, Bristol, Cardiff, Manchester and Newcastle-upon-Tyne, and the staffs of these centres put firms in touch with sources of information. The contact was made by actual visits from the research centres and by the normal Press reports and brochures. In answer to another question, Mr. Nicholls said that from the research reports on social and psychological research in industry, the Department, with the agreement of the Medical Research Council, had selected twelve projects as suitable for presentation in a short and popular form, and three of these had already been published by H.M. Stationery Office.

International Cultural Affairs

In a debate on the international situation in the House of Lords on May 4, Lord Aberdare stressed the value of university scholarships and exchanges in furthering international understanding, and urged the Government to consider increasing its present grant of £6,000 a year to the European Cultural Fund which at present has an income of only £32,000 a year. Lord Lansdowne, in replying for the Government on the debate, made no comment on this proposal, which was also advanced in an adjournment debate in the House of Commons on May 1. In the House of Commons, Mr. R. Allan, the joint Under-Secretary of State for Foreign Affairs, said that the Government was playing its part in the cultural work of the Council of Europe and was anxious to take it further. It did not exclude the possibility of a further voluntary government contribution, but wished to see first what could be done from private sources, as had been suggested by Mr. H. Delargy and Mr. R. Russell in opening the debate.

Beit Memorial Fellowships

The Trustees of the Beit Memorial Fellowships for Medical Research in their report for 1958–59 announce that Sir Francis Glyn has been elected a Trustee and honorary treasurer of the Trust; that Dr. Honor B. Fell has been appointed to the Advisory Board in place of Prof. J. H. Gaddum, who retires after fifteen years service; and that Sir Roy Cameron has been appointed secretary of the Trust in place of Prof. A. A. Miles, who retires from the secretaryship after seven years service.

The following elections have been made.

Junior Fellowships. Dr. W. D. Stein, to study the mechanism of specific transport systems across cell membranes at the molecular level, with special reference to the components concerned in the movement of glycerol across the human red blood cell membranes; at the Department of Colloid Science, University of Cambridge. Dr. G. Burnstock, to study the action of drugs on smooth muscle and the effect of autonomic nerve stimulation on the membrane potential recorded from smooth muscle cells; at the Department of Pharmacology, University of Oxford. G. L. Asherson, to study the causation of rheumatoid arthritis, systemic lupus erythematosus and other diseases in which antibodies against human and animal tissue can be detected; at the Rheumatism Research Unit (Medical Research Council), Canadian Red Cross Memorial Hospital, Taplow. E. R. Huehns, to study the hæmoglobins and the non-hæm proteins in normal and abnormal human red blood cells, with the view of distinguishing thalassæmia from the hæmoglobinopathies; at the Department of Biochemistry, University College, London. C. T. G. Flear, to study sodium–potassium exchange in tissues during induced congestive heart failure, and its bearing on the therapy of congestive heart failure in man; at the Department of Experimental Medicine, University of Cambridge.

Fourth Year Fellowships. T. F. Slater, to continue the study of the enzymic constitution of the rat mammary gland in relation to lactation; at the Department of Biochemistry, University College, London. Dr. J. R. Tata, to continue the study of normal and abnormal pathways of metabolism of thyroid hormones; at the National Institute for Medical Research, Mill Hill, London.

Presenting Science to the Public

An article by Prof. P. M. S. Blackett, reprinted from *Progress* of May 1958, appears under the title "The British Association Looks Ahead" together with two short notes on presenting science to the public in *The Advancement of Science* for March 1959. Prof. Blackett, starting with a brief historical survey, indicates some of the ways in which the British Association is seeking to play a wider part in the interpretation of science to the nation, and the three main aspects of modern science with which the Association must concern itself in so doing. The following note describes the work of the three area committees established at Newcastle, Durham and on Teeside, the lecture service, particularly for school audiences, the educational programme for young people under sixteen and the rapid development of the work of the Metric Committee and of the study group on the education of the graduate scientist in schools and universities. The third note describes the progress made in the preliminary survey of existing visual aids in relation to the Young People's Programme requested by the Visual Aids Committee in November 1958. The Young People's Programme is based on three main assumptions: that the most effective single weapon would be a magazine designed to present science attractively and authentically to young people; that it is also necessary to give the schools all possible help; and that the Science Clubs will require all possible assistance, including visual aids. It is believed that the Association would perform a major service by providing an impartial survey which outlined the role of existing agencies, published comments by those working in the field on the use and suitability of existing aids; and recommended, after consultation with existing agencies and individual experts, action to promote the better use of the material available as well as the production of new material.

Lecture Theatre proposed for the Royal Aeronautical Society

The Hyde Park Corner reconstruction scheme has provided the Royal Aeronautical Society with a unique opportunity for building a much needed lecture theatre at the back of its headquarters at

4 Hamilton Place, London, W.1. The new Apsley carriageway cutting across the corner of the Park is to be started soon and will give access to the site, but only while the road is under construction. The Society has seized this chance to launch an immediate appeal for the £150,000 needed to build and furnish a theatre seating more than 300. The detailed plans are completed and open to inspection. All planning permissions are assured and it is hoped to start work this September. Donations should be sent to the Secretary of the Society at the above address.

Ultrasonic Vibrations at 10,000 megacycles

An announcement by the International General Electric Co., of New York, reports that one of its scientists, Dr. E. H. Jackson, has been able to produce ultrasonics at the enormous frequency of 10,000 megacycles per second. Up to the present, the limit of frequency has been about 200 megacycles per second, obtained from one of the high harmonics of a thin slice of quartz, excited piezoelectrically. Details of Dr. Jackson's method are not given, but it appears that a quartz crystal is combined with a cavity resonator in such a way as to excite it at a high frequency. The usual difficulty with such a device is to avoid the crystal jumping from one harmonic to another, but to prevent the ultrasonic energy degenerating into that associated with thermal vibrations in the material, the crystal is kept at 2° K. It is proposed to use the source to investigate the energy-level of atoms and the interactions of electron spins in a crystal lattice. Another useful application—if the vibrations can be kept 'pure'—should be to study the absorption and velocity of ultrasonics in fluids with the view of finding very short relaxation times in the transfer of energy between the degrees of freedom of the molecules.

South African Museum

The success of a museum as an educational centre is to a large extent dependent on a competent professional staff. The report of the South African Museum for 1957–58 (pp. 19. Cape Town: South African Museum, 1958) indicates that three posts for professional officers and a taxidermist which had been allowed to lapse have been revived and a new post of historian established. It is hoped that the creation of the latter post will lead to the formation of a Cultural-historic Museum in Cape Town. A new store has been built and the Museum is now in a position to accept historical material for safe keeping and subsequent exhibition. Unfortunately the staff are so fully occupied with normal curatorial work that they have little time for research, a function which is essential for the full development of a museum. The report includes notes on five new inscribed stones recently discovered on the site formerly occupied by the General Post Office in Cape Town.

A New Field Centre

The Field Studies Council is planning to open a sixth Field Centre during 1959. In co-operation with the Herbert Whitley Trust, a building and land are being acquired at Slapton in South Devon, and, in the first place, it is hoped to provide facilities for about thirty students. The Council has designated Mr. Ian Mercer, formerly assistant warden at Juniper Hall Field Centre, to the warden's post at the new centre. The property is situated at the seaward end of Slapton village about 400 yd. from the shingle of Start Bay. Behind the shingle bank are two large freshwater lakes—the Leys—which, together with Slapton Wood and France Wood, constitute a Nature Reserve which will be leased to the Field Studies Council by the Herbert Whitley Trust. There is considerable opportunity for biological fieldwork. It is hoped that the Centre can be opened for small parties in the near future and more fully from July 1, 1959.

Besides the new Centre, the annual report for 1957–58 (pp. 28 + 4 plates. London: Field Studies Council, 1959) describes the continued growth and public demand for the existing Centres. Unlike previous issues, the annual report contains no scientific papers. In future, these are to be published independently under the new title, *Field Studies*. The first issue will include papers on the mollusca of the Flatford area; the insects of the Malham area; the geography of the Alberbury breccia; and the geomorphology of the Tillingbourne.

Architectural Science Review

Building is one of the traditional occupations of mankind which has become the subject of organized scientific inquiry only in comparatively recent times. In the early stages of research on building, attention was concentrated on the materials and constructions used, but latterly increased attention has been given to the overall problems of design. It is precisely with the scientific basis of architecture in the narrow sense of design for function that the new Australian journal, *Architectural Science Review*, is concerned (**1**, No. 1. Pp. 56. Three issues per year. Annual subscription, post free, 42*s*. (Australian); single copies, 15*s*. Academic Press Proprietary, Ltd., Sydney, Australia). The general scope of the *Review* is illustrated by the papers in the first issue and by the titles proposed for the second. In the first issue there are papers concerned with thermal comfort zones, the weathering of buildings (with particular reference to curtain walls), the design of structures with the aid of models, building in the tropics, and daylighting design. In addition, a selective bibliography on climate and architecture is given. For the second issue, papers on the Australian climate, on lifts and escalators, and on high-alumina cements are proposed, in addition to two further papers on lighting and insolation. The *Review* promises to provide a focus for the publication of researches which at present are scattered in numerous scientific and architectural journals. A new journal covering the field is to be welcomed, and it may well attract papers from outside Australia.

Kanamycin

The New York Academy of Sciences has recently published, in the form of a monograph, laboratory and clinical results obtained with kanamycin in various centres in North and Central America (*Ann. N.Y. Acad. Sci.*, **76**, 11; 1958. Article 2: The Basic and Clinical Research of the New Antibiotic, Kanamycin. By Maxwell Finland and 93 other authors. Pp. 17–408). Kanamycin is yet another *Streptomyces* antibiotic, which was discovered by H. Umezawa and co-workers of Tokyo. Obtained from a new species *Streptomyces kanamyceticus*, kanamycin is basic and water-soluble, closely related chemically to neomycin and has some features in common with streptomycin; it consists of two amino-sugars linked glucosidally to 2-deoxystreptamine.

In vitro, kanamycin is active against many common pathogenic aerobic Gram-positive and Gram-negative bacteria and *Mycobacteria*, but some *Pneumococci*, most *Streptococci* and *Pseudomonas* are resistant. Anaerobic organisms, yeasts and fungi nearly all show high resistance. Resistance to kanamycin induced in *Staphylococci* and in *E. coli* is accompanied by complete cross-resistance to neomycin and paromomycin and by partial cross-resistance to streptomycin, but no cross-resistance to unrelated antibiotics. Clinical results show that, given intramuscularly, the drug is effective in staphylococcal infections, gonorrhea, anthrax, and in many infections of the urinary tract, particularly when resistant to other antibiotics. Given orally, it inhibits aerobic intestinal bacteria. Alone, it is of doubtful value in tuberculosis, but is claimed to have some effect with *p*-aminosalicylic acid. The major toxic effects are on the kidney and eighth cranial nerve, but the renal toxicity is less marked than that of neomycin and the adverse vestibular and auditory effects are less than those obtained with streptomycin.

The Royal Institution : Officers

At the annual meeting of the Royal Institution, held on May 1, the following officers were elected : *President*, Lord Brabazon of Tara ; *Treasurer*, Mr. W. E. Schall ; *Secretary*, Sir Harold Spencer Jones ; *Managers*, Dr. T. E. Allibone, Dr. H. D. Anthony, Mr. F. G. Brown, Dr. A. G. Gaydon, Prof. A. Haddow, Mrs. H. K. Hawkes, Dr. H. Heywood, Dr. R. Holroyd, Mr. E. Ironmonger, Prof. L. A. Jordan, Mr. J. Lawrie, Sir Ben Lockspeiser, Mr. J. A. Oriel, Mr. H. P. Rooksby, and Mr. P. H. Schwarzschild ; *Visitors*, Mr. A. D. Baynes-Cope, Prof. H. Dingle, Dr. D. H. Follett, Mr. A. J. Haselfoot, Mr. S. Rees Jones, Mr. W. C. Lister, Miss C. M. McDowell, Mrs. J. E. Milton, Mr. F. A. Mitchell, Mr. N. P. W. Moore, Mr. J. D. Peattie, Mr. F. Y. Poynton, Mr. N. Shepherd, Dr. P. C. Spensley, and Dr. N. Stuart.

University News : Birmingham

The Council of the University, subject to the concurrence of the Senate, has gratefully accepted the offer of a contribution of approximately £140,000 spread over seven years for the purpose of enlarging and developing the Graduate School of Highway and Traffic Engineering, and for the establishment of a chair in the subject. The offer is made by a number of bodies concerned with road development, including the motor industry, oil companies, civil and engineering and surfacing contractors, insurance firms and motoring organizations.

The Nuffield Foundation has made a grant of £12,000 to the University, spread over five years from May 1, 1959, towards the cost of an investigation to be carried out in the Research Department of the Institute of Education into the placing, counselling and teaching of part-time students in a local technical college. The research will be under the direction of Mrs. E. C. Venables, at present part-time research fellow in the Institute of Education.

The following have been promoted to senior lectureships from October 1 : Dr. J. G. Valatin (mathematical physics), Dr. G. W. Greenlees (physics), Mr. R. H. Knight (physics), Dr. D. H. Whiffen (chemistry), Dr. V. G. Welsby (electrical engineering), Dr. V. Kondic (industrial metallurgy), Mr. P. T. Geach (philosophy), Dr. J. B. Finean (medical biochemistry and pharmacology). The following appointments have also been made : Dr. H. B. van der Raay, to be lecturer in physics ; Dr. R. W. Smith, to be lecturer in physical metallurgy ; and J. A. Nelder, head of the Statistics Section of the National Vegetable Research Station at Wellesbourne, to be a recognized lecturer in the Department of Pure Mathematics.

London

The following have been appointed to readerships tenable at the Imperial College of Science and Technology : Dr. F. G. H. Blyth (engineering geology) ; Dr. E. H. Brown (structural analysis) ; Dr. J. Edelman (enzymology) ; Dr. S. Eilon (production engineering).

Announcements

Under the statute of the Royal Society which provides for the election of persons who either have rendered conspicuous service to the cause of science or are such that their election would be of signal benefit to the Society, H.M. King Gustaf VI Adolf of Sweden has been elected a Fellow of the Royal Society.

The charter of the Middle East Technical University, Ankara, has been approved by the Grand National Assembly of Turkey. The conception of the University, which is intended to be an international centre of higher learning, was described in *Nature* of February 8, 1958, p. 382.

A symposium, arranged by the International Commission for Optics, in connexion with its fifth congress on Modern Systems for Detecting and Evaluating Optical Radiation, will be held in Stockholm during August 24–30. Further information can be obtained from Prof. E. Ingelstam, International Commission for Optics, Stockholm 70.

The summer meeting of the Science Masters' Association will be held in the Science Laboratories of the Durham Colleges during July 27–31. In addition to the usual programme of meetings and visits, there will be Publishers', Manufacturers' and Members' Exhibitions, and a discussion on "General Trends in Science Teaching in the Universities of the Commonwealth", introduced by Prof. W. B. Fisher. Further details can be obtained from the Meeting Secretary, W. H. Dowland, 93 Westbourne Road, West Hartlepool, Co. Durham.

Under the auspices of the International Union of Biochemistry, a symposium on Hæmatin Enzymes is to be held in Canberra, Australia, during August 31–September 4. The symposium is being arranged by the Australian Academy of Science, and participation is by invitation. The proceedings of the symposium are to be published by the Pergamon Press in a special volume. Further information can be obtained from Prof. R. K. Morton, Department of Agricultural Chemistry, University of Adelaide, South Australia.

An International Conference on Nuclear Structure will be held at Queen's University, Kingston, Ontario, during August 29–September 3, 1960. The conference, in addition to receiving support from the International Union of Pure and Applied Physics, will be sponsored in Canada jointly by Atomic Energy of Canada, Ltd., and Queen's University. The secretary of the conference is Dr. L. G. Elliott, Atomic Energy of Canada, Chalk River, Ontario, to whom further inquiries can be directed.

Erratum. In the article "A New Short-acting Thiobarbiturate", by Dr. M. E. Peel *et al.*, published in *Nature* of May 23, p. 1443, in Table 1 for compound B.137, R' should read Bu^{s}, not Bu^{i}.

DEPARTMENT OF HUMAN ANATOMY, OXFORD: NEW BUILDINGS

THE time devoted by medical students to the meticulous dissection of cadavers and the memorizing of a mass of anatomical detail has diminished considerably in Great Britain during the past half-century. It is now recognized that an encyclopædic knowledge of topographical anatomy is devoid of educational value and its practical application is restricted to surgical specialists and a few selected research workers. By contrast, a knowledge of the structure and functional role of the tissues which go to make up the body in subjects of all ages, of their reactions to stress, and to the wear and tear of everyday life, is acknowledged to be of both educational and practical value to physicians, surgeons, general practitioners and research workers alike.

This re-orientation in the role of anatomy as an academic discipline in Britain owes more to Sir Wilfrid le Gros Clark than to any other anatomist. F. P. Mall pioneered a similar movement at Johns Hopkins University in the United States of America in the early 1900's which was quickly accepted and exploited by such eminent scientists as George Corner, Herbert Evans and George Wislocki. Now, however, there is a tendency in the United States to regard anatomy as a part of biology almost divorced from medicine, and to appoint more and more teachers who have not had a medical training. The opening of the new Department of Anatomy in the University of Oxford (Fig. 1) is a milestone in the history of a reformation in England which has proceeded more slowly and which seeks to avoid this tendency.

Sir Wilfrid's genius has been to gather around him, and provide facilities for, people interested primarily in the changes which occur in the tissues of the human body in health and in response to trauma (and selected diseases) from conception to death from old age. This is not to say that experimental work on lower animals is not carried out in his Department; indeed, it is, but that, under his leadership, teaching and research are directed more towards the biology of man than of other animals. Sir Wilfrid has contrived to allow anatomy to evolve rather than denying it a place as an academic discipline or allowing it to become a home of lost biological causes. This he has achieved through his unique distinction both as an outstanding experimental neurologist and as an outstanding authority on primate anthropology which, incidentally, he regards as a hobby.

The subjects most strongly represented in the new Department are neuroanatomy, with special reference to vision, olfaction and common sensation. Modern methods of microscopy, including electron, reflecting, phase contrast and interference techniques, are also

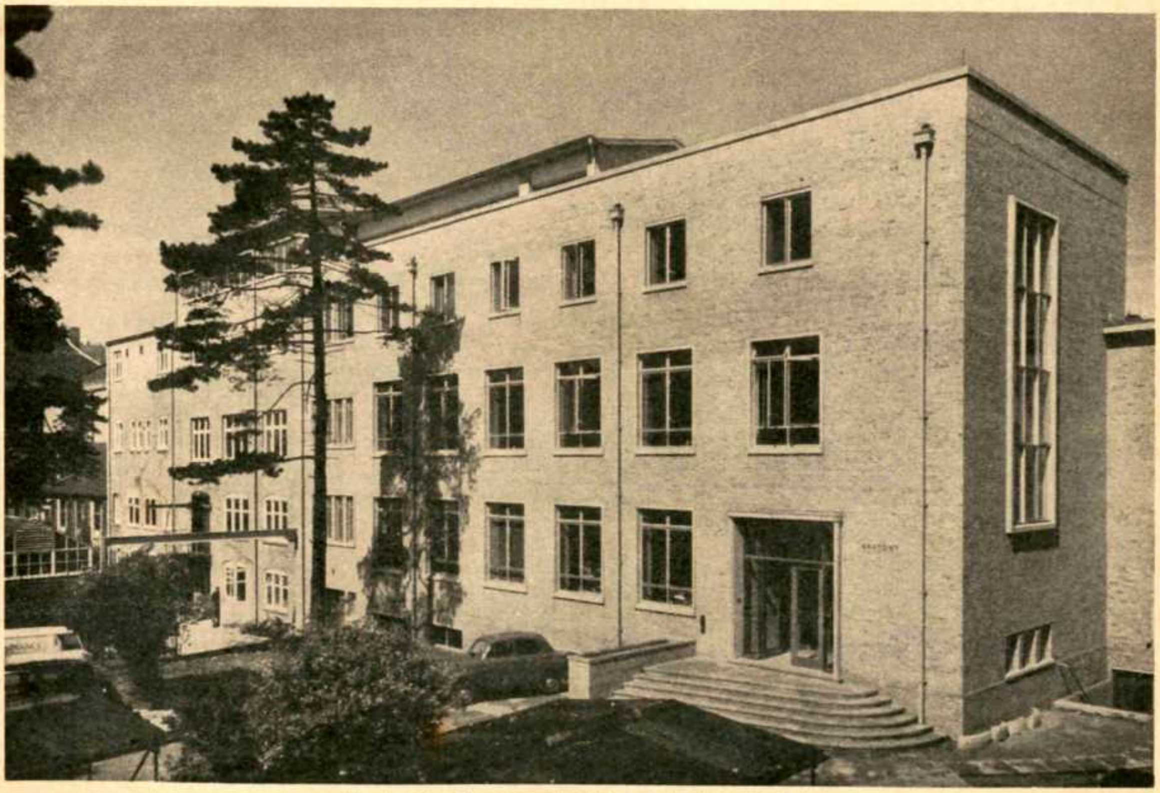

Fig. 1. New Department of Human Anatomy, Oxford

under active investigation. They are housed in special rooms in the basement of the building and are being used, among other things, to obtain quantitative data concerning the anatomy of individual living cells. The mechanics of muscular activity in man and in experimental animals are also being studied by a number of different methods, including strain gauge techniques and electromyography. Physical anthropology is also strongly represented and intensive work is being carried out on the adaptation of human subjects of different age and race to extremes of environmental temperature.

The old department has been entirely transformed from a mushroom growth of ill-suited, over-crowded research rooms, leading off from an old-fashioned dissecting room and a small museum, to a modern research laboratory adaptable to any field of biological study.

The essential features of the new Department are an extremely well lit, adequately ventilated and conveniently proportioned dissecting room. This can also be used for the study of surface and functional anatomy. It surmounts a large, well-equipped histological laboratory which in turn surmounts a basement containing an up-to-date embalming room, body store, and a room in which recently deceased persons can be viewed by relatives should the necessity arise. Close to this unit are a conventional lecture theatre, a small demonstration theatre and a departmental library. Beyond these is a commodious museum which can also be used as a study and reading room. This has evolved from the former dissecting room by a process of adaptation and the skilful use of modern methods to improve the interior décor of the old structure. Lying between the museum and the new dissecting room are the laboratories and offices occupied by the staff.

The staff includes a professor, two readers and four University demonstrators, each of whom devotes his time to a particular branch of anatomy, assisted by departmental demonstrators and postgraduate students reading for higher degrees. A few rooms which serve as combined laboratories and offices have been set aside for the use of temporary visitors from overseas. Housed and integrated with the rest of the Department is a Medical Research Council climatic and working efficiency unit which possesses an up-to-date climatic chamber. The Department also has a large well-equipped workshop for handling metal, plastics and wood, as well as a smaller instrument workshop. It also contains a large well-designed photographic department containing the most modern equipment which is capable of handling every kind of photographic problem. The animal house and operating theatre are on the roof of the building and conform to the highest modern standards. The individual research laboratories are simple yet quickly adaptable to different kinds of biological research with the minimum of expense. In particular, they are well lit and ventilated, and provided with a service panel encircling the room, having gas, electrical (direct and alternating current) and compressed-air outlets at intervals. The rooms are also provided with sinks having hot and cold water supplies. Three of the rooms contain, in addition, fume cupboards, and two rooms have voltage-stabilized alternating-current electrical outlets and dark-room blackout blinds. There is also a small light- and sound-proof room. The majority of the benches in these rooms are movable but strong, rigid, relatively light and fitted with plastic tops. They have been supplied in two standard heights, lengths and widths, and they can be fitted adjacent to the walls beneath the service panel. They can thus be moved from room to room according to requirements. A variety of units in two sizes containing drawers and/or cupboards have been provided for fitting beneath the benches. These can also be moved from room to room to suit particular requirements. These research rooms can therefore be adapted to serve such diverse techniques as standard histology, tissue culture, biochemistry and biophysics. An adequate number of lavatories, wash basins, locker and store rooms have also been provided.

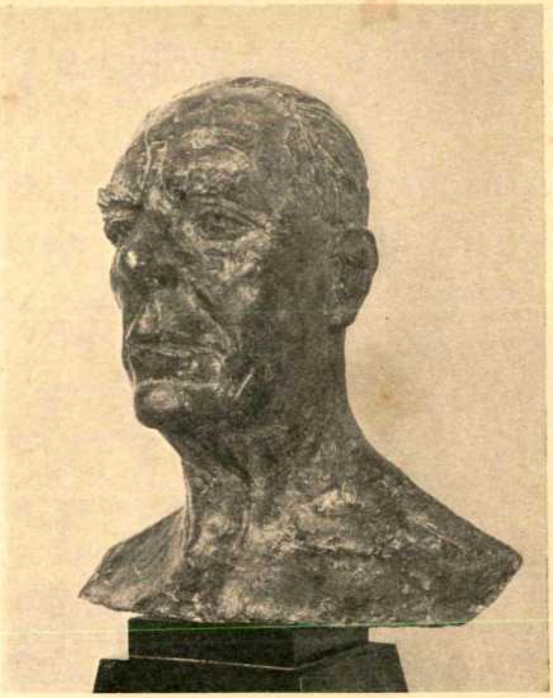

Fig. 2. Bust by Sir Jacob Epstein of Sir Wilfrid le Gros Clark

Sir Wilfrid's friends and colleagues have recognized that his genius has set him among the immortals. But as the regius professor of medicine at Oxford, Sir George Pickering, said when he opened the new building on March 16: "Immortality as is commonly conceived is relative rather than absolute and, since what is generously called the growth of scientific literature, may obscure masterpieces like le Gros Clark's writing, his friends thought it right to secure his more permanent immortality by asking Sir Jacob Epstein to create a portrait bust". The opening of the new Department comes just twenty-five years after Sir Wilfrid was appointed Dr. Lee's professor of anatomy and Fellow of Hertford College in the University of Oxford. It is therefore very fitting that a work of this kind should have been commissioned from a great sculptor in honour of Sir Wilfrid, to be permanently housed in the Department which his vision has done so much to create.

The bronze portrait bust of Sir Wilfrid le Gros Clark is sited in the entrance hall of the new building in a quiet and dignified setting but where it can be seen and examined for the work of art which it is (Fig. 2).

G. Weddell

U.S. NATIONAL ACADEMY OF SCIENCES

Centennial Gift from the Equitable Life Assurance Society

THE U.S. National Academy of Sciences, the president of which is Dr. Detlev Bronk, is to receive a gift of a million dollars from the Equitable Life Assurance Society of the United States as a contribution to the nation's welfare during the Society's hundredth anniversary. The Academy itself celebrates its centennial in 1963.

The gift will provide for the erection of a Hall of the Life Sciences, in which will be housed the many scientific activities of the Academy and its National Research Council in the fields of biology and medicine.

The National Academy of Sciences is a private, non-profit organization electing its own members from among leading scientists of the United States. The Academy was established in 1863, under a Congressional Charter signed by President Lincoln, to advance science, further human welfare and advise the Federal Government on scientific and technical matters.

The National Research Council was organized by the Academy in 1916 at the request of President Woodrow Wilson, as a part of the Academy, in order to enable representatives of the major scientific and technical societies to co-operate in the efforts of the Academy in the service of science and the national welfare.

The Academy–Research Council is the principal agency through which American scientists participate in co-operative international scientific undertakings such as the International Geophysical Year and other activities of the international scientific unions.

The present building of the National Academy–Research Council, which is generally considered to be one of the most beautiful in Washington, was constructed in 1924 with funds provided by the Carnegie Corporation of New York and was dedicated thirty-five years ago by President Coolidge. It is situated on Constitution Avenue, adjacent to the New State Department Building now under construction, and facing the memorial to Abraham Lincoln, who was the founder of the Academy.

Architects for the new Hall will be Harrison and Abramovitz, who have been associated with the design of many of the notable buildings of America, such as the Rockefeller Center, the Lincoln Square project in New York, and the United Nations building.

Dr. Bronk made the following comment on the Equitable gift: "Erection of this new Hall of the Academy to house the medical and life sciences will be of great value to our nation. It is eminently appropriate that the Equitable Life Assurance Society thus contribute to the work of the Academy, for we are both private organizations devoted to the public welfare.

"Both organizations are deeply concerned with the furtherance of those sciences which prolong life and increase health. We are both national in scope. In the beautiful centre of our national capital, the Hall of the building provided by the Equitable centennial gift will symbolize your service to the welfare of the people of our nation and will enable us to increase our service as we, too, begin our second century".

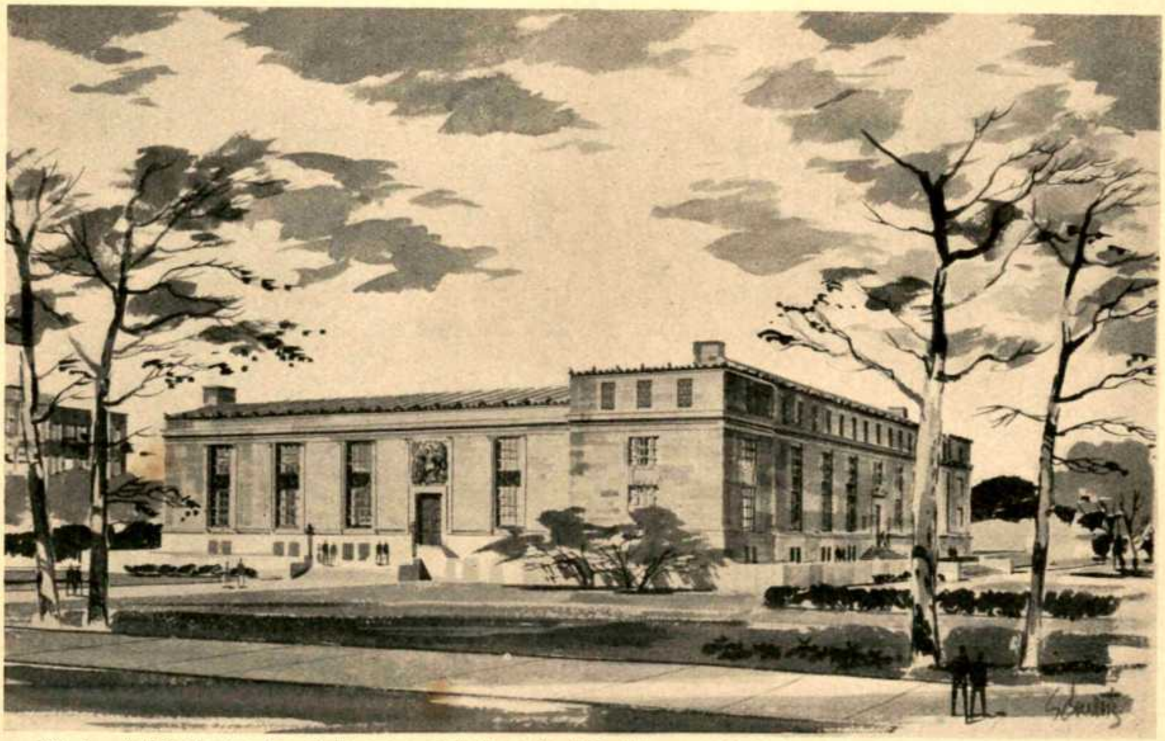

Fig. 1. Architect's drawing of the proposed Hall of the Life Sciences, U.S. National Academy of Sciences, provided by the Equitable Life Assurance Society

When the Academy's building was erected in 1924, it was planned to accommodate additional wings as the need developed and funds became available. With the greatly increased scope of the Academy's work, more space has been urgently needed, and many activities of the Academy–Research Council have had to be housed in widely scattered locations throughout Washington.

The work of the Academy–Research Council is carried on by more than a thousand committees comprising scientists who voluntarily give their time and represent all fields of science; they are served by a full-time staff of more than 1,100. More than 10,000,000 dollars a year is provided for the work of the Academy by private foundations, contracts and grants from the Federal Government, and income from the Academy endowment of approximately 7,000,000 dollars a year.

Elections

Dr. Hugh L. Dryden, deputy administrator of the National Aeronautics and Space Administration, has been elected to a second four-year term as home secretary of the U.S. National Academy of Sciences.

Dr. Roger Adams, research professor of chemistry, University of Illinois, and Dr. William V. Houston, president of Rice Institute, have been elected members of the Council. The two councillors who are retiring are Dr. I. I. Rabi, professor of physics, Columbia University, and Dr. F. E. Terman, professor of electric engineering, Stanford University.

As members of the Council of the Academy, the home secretary and the two new councillors will share responsibility for the general conduct of the Academy and its National Research Council.

The following have been elected to membership of the Academy:

Dr. Philip H. Abelson, director of the Geophysical Laboratory, Department of Terrestrial Magnetism, Carnegie Institution of Washington.

Prof. Walker Bleakney, Brackett research professor in Princeton University.

Prof. David Bonner, professor of microbiology, Yale University.

Prof. Tom Bonner, professor of physics, Rice Institute.

Dr. Walter Brattain, research physicist, Bell Telephone Laboratories (on leave with the National Defense Research Committee, Columbia University).

Prof. Leo Brewer, professor of chemistry, University of California at Berkeley.

Prof. Frank Brink, dean of graduate studies, Rockefeller Institute.

Prof. Jens C. Clausen, Division of Plant Biology, Carnegie Institution of Washington, and professor of biology, Stanford University.

Prof. Samuel Eilenberg, professor of mathematics, Columbia University.

Prof. John D. Ferry, professor of chemistry, University of Wisconsin.

Prof. Kurt O. Friedrichs, professor of applied mathematics, New York University.

Prof. Hiram B. Glass, professor of biology, Johns Hopkins University.

Prof. M. J. Herskovits, professor of anthropology, Northwestern University; former visiting professor, Graduate School, University of Illinois.

Prof. Herman M. Kalckar, professor of biochemistry, Johns Hopkins University.

Prof. Konrad B. Krauskopf, professor of geology, Stanford University, and geologist, U.S. Geological Survey.

Prof. I. Michael Lerner, professor of genetics, University of California at Berkeley.

Dr. Rudolph L. B. Minkowski, Mount Wilson and Palomar Observatories, and research associate, California Institute of Technology.

Dr. Harry F. Olson, Radio Corporation of America Laboratories.

Prof. C. Pfaffmann, professor of psychology, Brown University.

Prof. Richard J. Russell, professor of physical geography, and dean of the Graduate School, Louisiana State University.

Prof. John A. Simpson, scientific consultant, Argonne National Laboratory.

Prof. Dean S. Tarbell, professor of organic chemistry, University of Rochester.

Prof. Henry Taube, professor of chemistry, University of Chicago.

Prof. James A. Van Allen, professor of physics, State University of Iowa.

Prof. Cecil J. Watson, professor of medicine, University of Minnesota.

Prof. Gregor Wentzel, professor of physics, University of Chicago.

Prof. Fred L. Whipple, director, Smithsonian Astrophysical Observatory (a close associate with Harvard College Observatory).

Prof. William B. Wood, jun., vice-president of medical affairs, and professor-elect of microbiology, Johns Hopkins University.

Prof. Clarence M. Zener, director, Westinghouse Research Laboratories.

Dr. Raymond E. Zirkle, professor of radiobiology, University of Chicago.

CHARACTERISTICS OF THE ANTARCTIC ICE-SHEET

THE Royal Astronomical Society Geophysical Discussion of February 27 was held jointly, in the Society's rooms at Burlington House, with the British Glaciological Society. This combining of interests by the two organizations was matched by the bringing together of the theoretical with the directly practical interests, for the main speakers were Dr. J. F. Nye (chairman) on one hand, and M. B. Imbert, Mr. J. G. D. Pratt and Dr. H. Lister on the other. Dr. Nye's important contributions to the study of ice-sheets are well known and, perhaps more than anyone, he has shown clearly what physical properties should be measured by the expeditions that go to make the necessarily difficult and sometimes hazardous experiments; and he has put together the numbers of the problem so that the field men can plan their experiments and know when they are getting a reasonable answer.

M. Imbert has for many years been principal assistant to Dr. Paul Emile Victor of the Expéditions

Polaires Françaises, and Mr. Pratt is a seismologist of world-wide experience in the British Petroleum organization. They both had returned recently from Antarctica and were able to describe some of their results, both seismic and gravitational, fresh from the detailed analysis that awaited their return home. As opposed to the static problem of what is there now, Dr. Lister studies the mechanism of deposition of snow and its formation into an ice-sheet, together with the dynamical aspects and the history of these phenomena. Dr. Lister and Mr. Pratt were members of Sir Vivian Fuchs's Commonwealth Trans-Antarctic Expedition, and M. Imbert was leader of the French team in Antarctica for the International Geophysical Year.

Dr. Nye explained that the behaviour of an ice-sheet is governed by two opposing forces: the weight, which tends to squeeze the ice out sideways, and the resistance to outward flow provided by the bed. These two forces are essentially in balance.

The properties of the ice depend upon the temperature distribution in the ice, and this in turn is affected by two main sources of heat. Heat is flowing from the Earth itself, presumably in the absence of volcanic activity, at the normal rate, and it is also developed by friction as the ice moves over the rock bed. If the effects of transverse convection are ignored, theory suggests that both sources of heat are tending to make the lower layers of ice warmer than the upper ones. The ice will therefore become more plastic at the bottom than at the top. The shear stress tending to move the mass of ice is known to increase linearly with depth in the ice, and therefore the shear distortion will take place predominantly in the lowest layers. It does not matter very much if, in the analysis, the distortion is regarded as slipping on the rock bed rather than very intense shear in the lowest layer.

The movement of the ice-sheet is outwards towards the unconstrained perimeter, and the calculated strain rates at the ice – rock interface are of the order of about 10^{-2} per annum. This is much higher than the slow rate (about 10^{-4} per annum) of the squeezing down movement of vertical compaction, which is partly or entirely compensated by the addition of new material by snowfall. However, it is the weight of accumulated snow that ultimately provides the driving force for the ice-sheet, and the connexion between the vertical and the outward strains in the ice is such that, in a steady state, the outflow is just sufficient to balance the accumulation.

A simple model of the ice-sheet shows that the steady-state thickness of the ice is proportional only to the fifth or sixth root of the accumulation. This means that the height of the ice-sheet is very insensitive to even long-period changes of accumulation, and it is for this reason that calculations of the equilibrium form of an ice-sheet can be made with fair accuracy without a knowledge of the accumulation. The relevant measurements that are required, therefore, from the field experiments are a knowledge of the topography, the thickness of the ice, and the past and present rates of accumulation.

M. Imbert's results covered a traverse, 300 miles long, running inland from the French International Geophysical Year base in Adelie Land. In the 1957–58 season seventy-five shots were fired to obtain seismic reflexion results at twenty-five stations. The recording gear covered the nominal frequency-range of 600 c./s., but as with most Arctic and Antarctic seismic investigations it was found desirable to put the charge as deep as possible into the layers of poorly compacted snow. A charge of 1 kgm. of high explosive at a depth of 18 m. was found to give readable reflexions, and the quality of a number of 'typical records' that were shown were certainly excellent. Mr. Pratt managed to bury some of his charges to a depth of 12 m., but this was not really deep enough, and in many cases lack of time forced him to be content with surface shots. It is noticeable that the reflexions do not stand out so clearly as some of M. Imbert's, but care must be taken in ascribing record quality entirely to the effect of depth of charge, since some results from the British North Greenland Expedition show that unexplained phenomena deep down in the ice also have considerable effect on the strength of reflexions.

The French seismic profile was supplemented in 1958–59 by seventy gravity stations, and the topography of the surface of the ice-sheet was measured to an accuracy estimated at 15–20 m. Barometric heights were backed up by estimates of atmospheric pressure obtained from radiosonde measurements. The mean height of bedrock was 40 m. below sea-level along the traverse, but elevations and depressions of several hundred metres were observed about this mean. If h km. is the height of the surface above sea-level at point x km. inland, then the surface of the ice fitted the ellipse:

$$\left(\frac{h}{2\cdot 68}\right)^2 + \left(\frac{550 - x}{550}\right)^2 = 1$$

with a root-mean-square error of ± 25 m.

The profile presented by Mr. Pratt covered the 2,000-mile course of the Commonwealth Trans-Antarctic Expedition. The seismic picture was different from that of other observers in that the ice – rock interface was, except for two troughs on the Weddell Sea side of the South Pole, well above (about 1,500 m.) sea-level. This may be accounted for on the Ross Sea side of the pole by the fact that the course of the expedition lay over the foothills of a known mountain range.

The gravity measurements were checked at the South Pole and at the Ross Sea, but the uncertainty about height in between gives a possible error of 25–50 mgal. The estimated error due to drift is much less than this, of the order of 5 mgal. The gravity results support the seismic picture, and Bouguer anomalies have been drawn assuming the profile found from the seismic measurements, together with a rock density of 2·1 gm./cm.^{3}. There is a large anomaly of − 200 mgal. which cannot be explained away by the uncertainties of the measurements. It appears that the ice-sheet must have been subject to a much greater loading in the past than is effective to-day, and that the Antarctic land mass is, like Scandinavia, tending to rise. It would be most interesting to make a careful series of elevation measurements, but the technical difficulties of such observations from a continent fringed with ice are considerable.

A single American seismic result at the South Pole differed from the several that Pratt obtained in the vicinity of the pole, and this was explained by the inherent difficulty of interpreting an isolated record taken under the difficult conditions pertaining to ice-sheets. Pratt had gained a great deal of experience by the time the pole was reached, and the polar observation was a continuation of a whole series of reflexions on the profile hundreds of miles long, so that, apart from the fact that several independent results were obtained, Pratt's value must be accepted rather than the much deeper American figure.

A short refraction line at the South Ice station, 300 miles inland from the main Shackleton base, showed that the velocity in the 80–90 metre thick surface layer varied from 0·5 to 3·96 km./sec., in agreement with observations in other parts of the world. An interesting point emerged from the refraction results. The line ran over undulating snow, but there was no sign on the record of the surface variations in height. It must be assumed, therefore, that the troughs of the undulations consist of lower-velocity material than do the humps. Some shots fired on the ice-shelf yielded reflexions from the sea bed, but not from the bottom of the ice. This is a familiar experience with Antarctica geophysicists, but Pratt has pointed out that a unique solution of ice thickness can be obtained from the travel time of waves reflected from the sea-bed.

Dr. Lister's simple method of following the accumulation of snow by laying down strings at fortnightly intervals and afterwards checking their profile by digging was supplemented by counting the years indicated in the stratification caused by seasonal changes in climate. Pits and drilled cores at South Ice enabled Lister to look back to the year 1895, and across the continent twenty bore-holes reached back twenty years and sixty more were deep enough to include the deposition of the past five years. Along the central portion of the traverse followed by the Trans-Antarctic Expedition the deposition-rate was found to be fairly constant at 8–9 cm. water equivalent a year. This is rather higher than the 6 cm. found by the American observers at their South Pole Base, but may be accounted for by the fact that much of the expedition's route followed a trough in the surface topography. The accumulation increases to about 25 cm. water equivalent at the edges of Antarctica, and Lister calculates a deposition-rate of 13·1 gm./cm.^{2}/year as an average over the whole continent. The wastage is assessed at 10·1 gm./cm.^{2}/year mainly made up of 5·0 melting, 4·0 icebergs, 1·0 evaporation and 0·1 deflation. It appears then, from the present-day observations, that there is a net gain of ice, a result (ignoring any time-lag) opposite to that indicated by the negative gravity anomaly. During the discussion it became apparent that the figures for melting and for loss by breaking off of ice-floes might be changed in the light of other observations, but in any event the present material balance was one that applied to decades rather than to the thousands of years (at least) during which changes in the ice-cap, sufficient to account for the gravity results, would be expected to take place.

Some of Lister's observations made it clear that precipitation favoured hollows rather than the crests of undulations, and that there was a migration of the crests with time. Nye raised the question of whether the presence of the undulations might affect the travel of the whole sheet, because their presence implies a big change of slope over a distance larger than the thickness of the sheet. There was clearly a mechanism here which could give local fluctuations of velocity and hence it would be very difficult to make sense of any isolated measurements of ice-sheet velocity. It is possible that the movement of the crests is only apparent, and is caused by the erosion of hard wind-blown snow at the crests of the undulations, with a simultaneous build-up of a new crest above the snow-filled troughs. Whether they are caused by aerodynamic or by hydrodynamic means, the undulations and sastrugi deserve further attention, and the results that have been collected recently should call forth a new advance on the theoretical side.

T. F. GASKELL

THE NATIONAL SCIENCE FOUNDATION

REPORT FOR 1957–58

MORE than half the eighth annual report of the National Science Foundation for the year ended June 30, 1958*, is occupied by appendixes listing the membership and staff of the Board, its committees and advisory panels, grants for basic research, fellowship awards, publications of the Foundation and others resulting from research grants and fellowships. The latter now runs to some 1,315 items, compared with 850 in 1956–57, and is arranged according to the several divisions of the Foundation. Fellowship awards during the year totalled 1,527, amounting to about 5·6 million dollars in value. Of these, 408 were in the biological sciences, 314 in physics and astronomy, 306 in chemistry, 206 in mathematical sciences, and 193 in engineering. Of the total, 1,084 were predoctoral, 227 postdoctoral and 216 in the science faculty programme for improving the quality of science teaching. Grants for research amounted to more than 19 million dollars, and of these 1,120 grants, 605, totalling 8,881,130 dollars, were in biological and medical sciences; 466 grants, totalling 9,507,825 dollars, in mathematical, physical and engineering sciences; and 49 grants, totalling 725,950 dollars, in social science. During the year, 190 scientists received grants, totalling 113,220 dollars, in support of travel to international scientific meetings, and the Foundation sponsored and provided partial support for thirty-four scientific conferences and symposia.

Reviewing the support given to basic research in the sciences, in the Division of Biological and Medical Sciences, the report stresses the clue to the control of tuberculosis provided by the study of the honey guide, a wax-eating bird found primarily in Africa, from the intestinal tract of which a wax-splitting bacterium was isolated that contains a protein which inhibits the growth of the tubercle bacillus in tissue cultures. Doubts have been thrown on the basic genetic axiom regarding the individuality of genes by the discovery that the gene in corn which produces colour in the kernel can be permanently modified by bringing it into combination with a particular partner gene. Results have been obtained suggesting that some plants may operate as a well-knit group or unit having a common physiology, and it has also been found that nerve growth factors similar to the tumour factors are present in the salivary glands of the mouse and rat, in snake venoms and in the venom of the Gila monster. Sex hormones have been found to control growth in the more primitive plants such as water moulds and ferns, and protein-like material has been produced by application of heat (170° C.) to mixtures of amino-acids. The discovery of a method for introducing sulphydryl and disulphide groups into proteins and protein-like molecules has permitted the physical, chemical and physiological characteristics of proteins to be altered at will. Deoxyribonucleic acid has been synthesized by adding an enzyme obtained from bacteria to a previously prepared mixture of nucleic acids, and in studies of the growth of *Brucella abortus* and *Diplococcus pneumoniae* addition of a mixture of bacterial deoxyribonucleic acid and deoxyribonuclease to growing cultures of these organisms had striking effects upon the selective establishment of virulent cells in an initially non-virulent population.

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* National Science Foundation. Eighth Annual Report for the Fiscal Year ended June 30, 1958. Pp. xv+246 (8 plates). (Washington, D.C.: Government Printing Office, 1959.) 1 dollar.

In the Division of Mathematical, Physical and Engineering Sciences, the report directs attention to the cloud-seeding experiments near Tucson, Arizona, where radar observations indicated that precipitation from larger seeded clouds was greater than from similar unseeded ones; to the development of a neurological instrument which enables ultrasonic waves to be used to cut out tiny regions of the inner brain without disturbing the inner structure; to a laboratory model of a stream which, used in conjunction with a high-speed motion-picture camera, has clarified the motion of individual sand grains in a flowing stream; to the laboratory confirmation of the hypothesis that pegmatites are relatively dry melts (magmas) and are closed physico-chemical systems, and that the giant crystals are formed during a 'second boiling'; to the development of techniques whereby free radicals are formed and immediately trapped on cold surfaces (− 424° F.); to the measurement of variations in the pull of gravity in Utah and Eastern Nevada which have permitted charting the major contours of the buried bedrock and given important clues to the configuration of the fault blocks and other structural patterns; and to the total stereospecific synthesis of several antibiotics and the production of a substance identical with natural rubber in physical characteristics by careful control of the spatial relations of the groups in the molecule.

In the Social Science Research Programme, electronic computers have been used to determine more quickly and sensitively the stages of the business cycle and to separate significant trends from temporary irregularities.

Besides the surveys made by the Foundation of the research and development effort of the United States and a brief report on the Conference on Research and Development and its Impact on the Economy called by the Foundation for May 20, 1958, the report summarizes the Foundation's activities in the International Geophysical Year. Apart from the fellowship programme already noted, the report deals at some length with the work which the Foundation is doing to improve science education. For this purpose the Foundation received a supplemental appropriation of 9 million dollars, which was used for the award of additional fellowships and to assist the attendance of more high-school science teachers at the summer institutes, of which 126 were held in 1958 in forty-seven States and three Territories. For 1959 the appropriation for the Foundation's educational programmes was increased to about 60 million dollars, but the educational implications of the report are discussed separately.

ENERGETIC COUPLING IN THE RESPIRATORY CHAIN

By Dr. POUL E. GLAHN and Dr. SIGURD O. NIELSEN

Carlsberg Laboratory, Copenhagen

THE important part played by the energetic coupling between substrate oxidation and adenosine triphosphate (ATP) synthesis (oxidative phosphorylation) in the energy economy of animal cells is well known[1]. The demonstration, *in vitro*, of energetic coupling between oxidation and reduction of carriers in the respiratory chain and adenosine triphosphate synthesis at present requires particulate preparations containing either mitochondria or multifunctional mitochondrial fragments. Experiments with such preparations indicate that the oxidation of reduced diphosphopyridine nucleotide (DPNH) by ferricytochrome *c* is coupled to the synthesis from adenosine diphosphate and free orthophosphate (P_i) of two moles of adenosine triphosphate per mole of reduced diphosphopyridine nucleotide oxidized[2,3] and that the oxidation of ferrocytochrome *c* by molecular oxygen is coupled to the synthesis of at least one mole of adenosine triphosphate (two moles being energetically possible) per two electrons transferred[3,4,14]. The detailed mechanism of this energetic coupling in the respiratory chain is essentially unknown in contrast to the coupling at substrate level[5] and its elucidation constitutes a major problem of contemporary biochemistry. In view of this fact and the great difficulty of experimental work with multifunctional, highly organized, and relatively ill-defined particles, it is amazing that no more speculation has appeared in the literature concerning the chemical nature of the coupling reactions, in particular the primary ones involving oxidation-reduction of respiratory carriers. It would appear that 'educated guesses' at the possible organic chemistry of these primary coupling reactions involving known or hypothetical respiratory carriers might be useful in the planning of new experimental approaches. The present article presents some ideas on the primary coupling reactions at all three phosphorylating sites between oxygen and reduced diphosphopyridine nucleotide. We feel less hesitant about publishing these views, which may eventually turn out to be wrong, because it has been possible to consider the primary coupling reactions at all four phosphorylating sites, including those at the cytochrome a_3- and substrate-levels, from a unified point of view.

The total number and location of carriers in the respiratory chain are still unknown, although it is generally agreed that diphosphopyridine nucleotide

(DPN), flavine adenine dinucleotide (FAD), cytochromes c, a, and a_3 are in the chain in the order given[6]. Tentative coupling schemes based on these established carriers have been proposed; for example, the reaction:

$$\text{DPNH} + X^{\bullet} + \text{FAD} \rightarrow \text{DPN} \sim X + \text{FADH}$$

has been suggested[1] as the primary reaction for the phosphorylation site in question. The whereabouts of the point of attachment of X to the nucleotide in the energy-rich compound DPN $\sim X$ is, however, left open.

Recently the organic chemistry of the coupling reactions has received some attention. Harrison[7] and Todd and co-workers[8] have suggested the phosphorylated form of a hypothetical, hydroquinone-type respiratory carrier as an intermediate which afterwards transfers its phosphate group to adenosine diphosphate following oxidation to the quinone-level. Similarly, Lindberg and co-workers[9] have postulated phosphorylation in the 2-position of the reduced *iso*alloxazine ring of reduced flavine adenine dinucleotide. Upon oxidation the phosphate group is transferred to adenosine diphosphate. In the case of hydroquinone phosphate experimental evidence is available that the phosphate group may actually be transferred to adenosine diphosphate after oxidation[8]. These examples bring out the essence of the coupling problem. When oxidized carrier A oxidizes reduced carrier B with the coupled synthesis of adenosine triphosphate, A_{ox} reacts directly with B_{red} only after combination of one or other of them with a group X (not necessarily phosphate) forming a 'low-energy' bond (standard free energy of hydrolysis $\Delta F^0 \simeq 0$). Upon reduction of A_{ox}—X by B_{red} or oxidation of B_{red}—X by A_{ox} the energy-rich compounds ($\Delta F^0 < -8$ kcal./mole)[10] $A_{\text{red}} \sim X$ and $B_{\text{ox}} \sim X$, respectively, are formed. In terms of standard oxidation potentials, E^0, this means that E^0 for the couple $A_{\text{ox}}—X/A_{\text{red}} \sim X$ is decreased by more than $8{,}000/96{,}500 \times z \times 0{\cdot}24$ V. compared with E^0 for the couple $A_{\text{ox}}/A_{\text{red}}$. This corresponds to 0·35 V. for a one-electron process ($z = 1$) and 0·17 V. for a two-electron process ($z = 2$). Similarly, E^0 for the couple $B_{\text{ox}} \sim X/B_{\text{red}}—X$ is increased by more than 0·35 V. for a one-electron process and 0·17 V. for a two-electron process compared with E^0 for the couple $B_{\text{ox}}/B_{\text{red}}$.

We shall now show how reduced diphosphopyridine nucleotide, reduced flavine adenine dinucleotide and ferricytochrome a_3 may combine through low-energy linkage with a nucleophilic group X^- (RS$^-$, RCOO$^-$, $H_2PO^-_4$, etc.) in such a way that the compounds DPN $\sim X$, FAD $\sim X$, and (Fe(II) cyt–a_3) $\sim X$ are energy-rich. The coupling schemes shown in Fig. 1 include the primary coupling reaction at substrate level[5] for comparison.

To see how these reaction schemes for diphosphopyridine nucleotide and flavine adenine dinucleotide transform the bond between X and the respiratory carrier from a low-energy bond on the left to an energy-rich bond on the right, the main bond systems in which resonance stabilization occurs are indicated in the formulæ (Fig. 1). Without going into details (for example, ref. 11) we may state that it follows from the uncertainty principle that the energy due to resonance of the molecule falls roughly as n^{-2}, where n is the number of bonds involved in a resonating bond system that resonates between structures of comparable energy. It follows that removing the amide carbonyl group of reduced diphosphopyridine nucleotide or the 4-carbonyl group of reduced flavine adenine dinucleotide from the resonating five-bond system to which it belongs (similar in both compounds) by substituting X for O occurs at the expense of only a small loss in resonance stabilization energy, because the molecules are still able to resonate over the four remaining bonds indicated in the formulæ. On the other hand, if the nucleotides are in the oxidized forms, and the same carbonyl groups are removed by substituting X for O, this occurs with a considerable loss in resonance stabilization energy which amounts to almost the whole of that of the amide group. The DPN $\sim X$ and FAD $\sim X$ bonds may, therefore, be considered as energy-rich. This conclusion is supported by a comparison of the standard oxidation potentials E^0 for the couples DPN/DPNH and acetyl-DPN/acetyl-DPNH (in the latter a methyl group is substituted for the nicotinamide amino-group). E^0 for acetyl-DPN is 0·072 V. higher than E^0 for DPN (ref. 12). The resonance stabilization energy in acetyl-DPNH is smaller than in DPNH $-$ X because resonance in the former but not in the latter involves a charge separation; it is therefore reasonable to suppose that E^0 for the couple DPN $\sim X$/DPNH — X might be at least 0·17 V. higher than that of the couple DPN/DPNH.

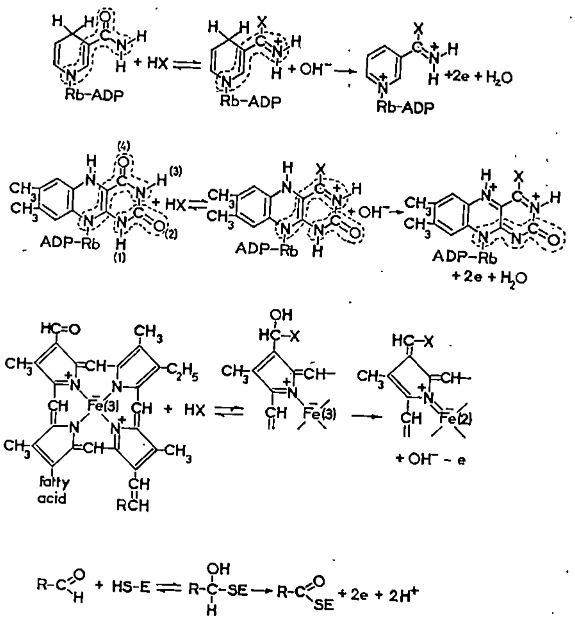

Fig. 1

It will be noticed that in the reaction schemes above it is the 4-position which combines with X, whereas Lindberg and co-workers[9] suggested the 2-position as the point of attachment. On the basis of considerations of resonance energy, like those above, the 2-position, however, appears to be less suited than the 4-position for engaging in the primary coupling reaction.

The number of electrons transferred in the energetic coupling reaction in the part of the respiratory chain between cytochrome c and oxygen is unknown[13]. A two-electron reaction involves either a higher oxidation state than ferricytochrome or a strong interaction between two cytochrome prosthetic groups, neither of which has been demonstrated. A one-electron coupling reaction might imply a maximal P/O ratio of 2 for the oxidation of ferrocytochrome c

by oxygen. Experimental ratios for this part of the respiratory chain are all smaller than one, possibly because of the experimental difficulties encountered. A ratio of 2 for the oxidation of ferrocytochrome *c* by molecular oxygen remains a definite possibility[14].

The reaction scheme proposed for the energetic coupling in the cytochrome system involves the formyl group of porphyrin *a* of cytochrome a_3 and is a one-electron process. The porphyrin *a* formula shown is the one given by Dixon and Webb[15], based on the work of Lemberg and co-workers[16]. A porphyrin formyl group is not present in cytochromes *b* and *c*. The formyl group tends to withdraw electrons from the rest of the iron-porphyrin complex[17] and there are various reasons, for example the high intensity of the α-band, for believing that there is much double-bond character in the iron-pyrrole nitrogen bond in ferrocytochromes *a* and a_3. The replacement of the formyl oxygen atom by X in ferrocytochrome a_3 may, therefore, involve a considerable gain in free energy so that (Fe(II) cyt–a_3) $\sim X$ is energy-rich. This suggestion is supported by available E^0 data for substituted iron phenanthroline complexes and for various hæmochromogens. In sulphuric acid Smith and Richter[18] found E^0 for iron 5-nitro-1,10-phenanthroline to be 1·25 V. compared with 1·06 V. for the unsubstituted iron 1,10-phenanthroline. At 30° C. and *p*H 9·63 the following E^0 values have been reported[19]: for the dicyanide hæmochromogens of coproporphyrin (all side-groups saturated) – 0·247 V., and of sphirographis porphyrin (a formyl and a vinyl side-group) – 0·113 V. The introduction of the electron-withdrawing groups NO_2 and CHO into the phenanthroline and porphyrin molecules increases the E^0 value for the iron complexes. The increase is less than the required 0·35 V. for a one-electron process, but this may tentatively be ascribed to the difference between porphyrins and other iron ligands in dicyanide sphirographis hæmochromogen, dicyanide coproporphyrin hæmochromogen, and cytochrome a_3.

Although porphyrin *a* is the prosthetic group of both cytochromes *a* and a_3 we prefer to write the primary coupling reaction with cytochrome a_3, because the E^0 span between cytochromes *c* and *a* is only 0·03 V., that is, too small for a coupled phosphorylation to occur[4]. The one-electron coupling reaction proposed is compatible with an overall P/O ratio of 1 for the oxidation of ferrocytochrome *c* by oxygen if molecular oxygen or hydrogen peroxide is reduced by one mole each of cytochrome *a* and cytochrome a_3 in a two-electron process.

The three primary coupling reactions proposed are analogous to the primary coupling reaction at substrate-level in so far as they involve a low-energy substitution at a carbonyl group and a gain in resonance stabilization energy on hydrolysis of the energy-rich form. The transfer of bond energy from $A_{\text{red}} \sim X$ or $B_{\text{ox}} \sim X$ to adenosine triphosphate may, therefore, also take place by analogous or similar mechanisms at all three phosphorylation sites in the respiratory chain. The suggested involvement of the oxidized forms of diphosphopyridine nucleotide and flavine adenine dinucleotide in energy-rich linkages is in agreement with labelled phosphate and adenosine triphosphate exchange experiments[3,20].

We are happy to acknowledge the interest and kind advice of Prof. K. Linderstrøm-Lang.

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USE OF RADIOACTIVE TRACERS IN STUDIES OF THE SHOOT APEX

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IN studies of morphogenesis at the shoot apex, hypotheses are often advanced which involve the transport of various substances, and their accumulation at specific sites, within the meristematic regions. Such hypotheses are difficult to test by means of standard physiological techniques because of the minute volumes of tissue involved. One possible approach to these problems is the use of radioactive isotopes, which have, indeed, already been successfully employed in studies of histogenesis in root apices[1] and, more recently, in the shoot apex of *Pinus*[2]. Previous work with radioactive tracers on apical meristems has been confined to autoradiography of sectioned material, thus restricting the area of tissue which it is possible to examine at any one time. A possible technique for obtaining autoradiographs of the whole surface area of intact or surgically treated shoot apices has been devised by us. This technique renders it possible, for example, to compare in a single film autoradiographs of visible leaf primordia, prospective leaf sites and the whole surface of the shoot apex, which could never all be viewed simultaneously in section. It is, however, applicable only to the investigation of phenomena occurring near the surface of the tissues.

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Shoot apices of *Dryopteris aristata* (*austriaca*) were used, both because this fern has already been the subject of extensive experimental investigation and because its apical region is of suitable form for the application of the technique described, in that it comprises a central apical cone and a number of small, spirally arranged leaf primordia which are not in contact (Fig. 1). The shoot apex was exposed to view by removing the older leaves and all scales. A cylinder of rhizome tissue, bearing the apical meristem at its tip, was then removed with a cork borer (9–12 mm. diameter), and trimmed to suitable length (5–10 mm.). The number of leaf primordia present, the stage of the plastochrone, and the direction of the phyllotactic spiral were noted, and the position of the next leaf primordium to arise (I_1) was marked. After allowing a 24-hr. recovery period, the cylinders of tissue were placed in a vertical position on filter paper moistened with the isotope solution, contained in a moist glass chamber. The isotopes used in this preliminary survey were phosphorus-32 (as a solution of orthophosphate) and 8-adenine sulphate labelled with carbon-14. An activity of 3–5 μc./ml. of solution (without the addition of carrier) was found to be suitable.

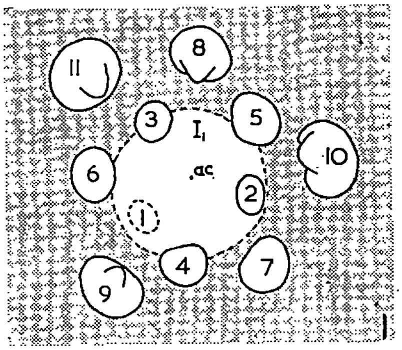

Fig. 1. Drawing of an apex of *Dryopteris aristata* similar to those from which the autoradiographs shown in Figs. 2 and 3 were obtained. Eleven young leaf primordia (P_1–P_{11}) are present; the position of I_1 (the next primordium to be formed) is also indicated. The apical cone is outlined with a broken line; the sub-apical region is stippled. *ac*, apical cell. (× 18)

The cylinders of tissue were removed from the dishes after an appropriate period of uptake, and thoroughly washed to remove any isotope solution on the surface. Thin, semi-circular slivers of tissue, about 4 mm. diameter and 1–2 mm. thick, bearing the apical meristem were excised from the cylinders and quickly affixed to small glass slides with 'Durofix'.

In a dish of water, small trapezium-shaped pieces of fast autoradiographic stripping-film (Kodak *AR* 50) were floated on to the surface of the apices and carefully orientated to allow subsequent recognition of the I_1 position. Excess water between the apex and the film was removed with filter paper; this considerably improved the subsequent fit of the film. The film was then quickly dried over the surface of the tissue with a stream of warm air from an industrial blower held at a distance of about 3 in. for 15 sec. The timing of this operation is important; with a shorter period of heating, the fit of the film was greatly impaired, whereas with more than 15 sec. heating, subsequent removal of the film from the tissue was rendered impossible. After this treatment the slide bearing the apex covered with film was placed in a light-tight container and maintained at a temperature of − 20° C. during the period of exposure. With phosphorus-32 an uptake period of 3–5 days with an exposure-time of 36–72 hr. usually gave satisfactory results, though longer periods of exposure were sometimes necessary (Fig. 3). Some differential blackening of the film was obtained after only 24-hr. uptake, with a long exposure period (11 days).

After exposure of the film, the slide was removed from its container, and the film was developed and fixed while still adhering to the apex. Since the film could not be examined satisfactorily with the opaque tissue beneath it, it was removed from the apex with fine forceps under water, and floated on to a slide. Areas of blackening on the film were then compared with the various regions of the apex, before

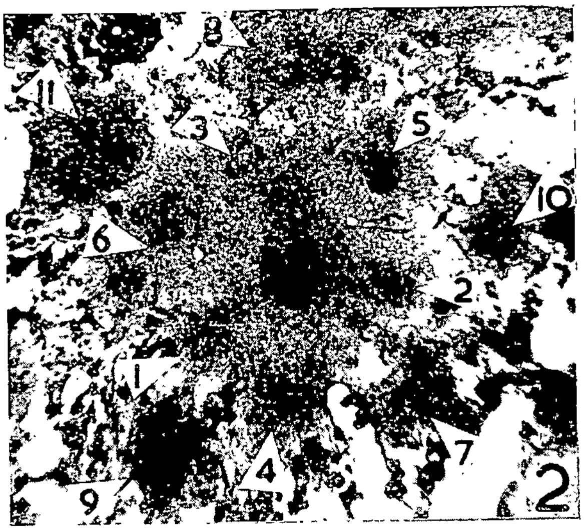

Fig. 2. Autoradiograph of an apex of *D. aristata* treated with phosphorus-32. Primordia 1–11 are present; P_8 and P_{10} were damaged. All the leaf primordia (arrowed) and the tip of the shoot apex (centre) are indicated by areas of blackening in the film. Totally dark areas, near the edge of the figure, are pieces of apical tissue adhering to the film; the film is also torn in places, leaving clear areas. Period of uptake of isotope, 6 days; film exposed for 40 hr. (× 20) (*Photo: G. Barker*)

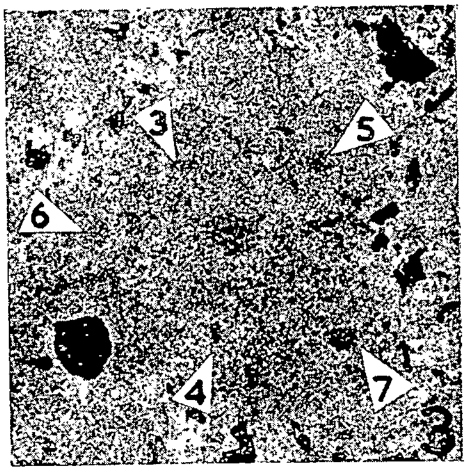

Fig. 3. Autoradiograph of an apex treated with phosphorus-32. Primordia 1–7 were present; P_1 (between 4 and 6) and P_2 (between 5 and 7) are not obvious in the film, but P_3–P_7 (arrowed) and the tip of the shoot apex (centre) are represented by blackened areas. Totally dark areas are pieces of tissue adhering to the film. Period of uptake of isotope, 3 days; film exposed for 14 days. (× 20) (*Photo: G. Barker*)

discarding the latter. Since the position of I_1 can be determined from the shape of the piece of film, and the direction of the phyllotactic spiral and the number of leaf primordia present were recorded at the beginning of the experiment, areas of blackening on the film may readily be assigned to the appropriate primordia or regions of the apex long after these tissues have been discarded.

The results thus far obtained indicate the potential usefulness of the method. Figs. 2 and 3 illustrate films obtained from apices treated with phosphorus-32. Considerable blackening due to silver grains is present over the whole area of film covering the tissue, as would be expected with an isotope of the range of phosphorus-32; but the blackening is not uniform. It is concentrated, in fact, at the positions of the leaf primordia; blacker areas can sometimes be detected down to and including the youngest leaf primordium, P_1 (Fig. 2). Damaged leaf primordia produce blackening comparable to that from intact primordia. Scales, scale primordia and those regions of the apex from which scales have been removed are recorded as paler areas in the film. The scope of the technique is not restricted to inorganic phosphorus-labelled compounds, but can be extended to organic carbon-labelled compounds, since comparable results were also obtained with adenine labelled with carbon-14. Films from control apices, placed on water containing no isotope, showed no appreciable blackening.

In conclusion, it should perhaps be emphasized that this method is still not without difficulties, and that a relatively small number of satisfactory demonstrations has been obtained from a considerable number of specimens. Moreover, these preliminary results have only demonstrated accumulations of tracer in visible primordia. The really effective contribution which we hope may be obtained from the method would be demonstrations of the accumulation of specific metabolites: (*a*) as a result of the presence of various experimental incisions, and (*b*) in the I_1, I_2 and even I_3 positions, thus providing evidence of the existence and approximate dimensions of centres of growth which are not as yet morphologically or histologically detectable. This aim has not yet been achieved, even in actively growing apices. However, in conjunction with existing experimental results and morphological techniques, it is felt that this method, when extended, may well throw light on these and other aspects of the physiology of the formative regions of plants, a difficult and little investigated field.

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RADIOCARBON MEASUREMENTS ON SAMPLES OF KNOWN AGE

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THE radiocarbon age method is at present based on the assumption that the ratio carbon-14/carbon-12 in atmospheric carbon dioxide has remained constant with time. The approximate validity of this assumption was originally demonstrated by Arnold and Libby[1], whose measurements of historically and tree-ring dated samples showed no significant deviations over the past 5,000 years (that is, none beyond 5 per cent of the age). Since then, other far more precise measurements have appeared in the literature[2–4], generally showing consistency between radiocarbon and absolute ages.

From a theoretical point of view, there are three possible reasons why the atmospheric ratio of carbon-14/carbon-12 might change with time: first, fluctuations in the rate of production of carbon-14; secondly, variations in the amount of stable carbon in the dynamic reservoir; and thirdly, variations in the pattern of inhomogeneous distribution of carbon-14 within the dynamic reservoir.

Recently the first and third possibilities have been discussed. Assuming that Thellier's[5] residual magnetism measurements of ancient French bricks typified the whole earth, Elsasser, Ney and Winckler[6] calculated that the greater magnetic field intensity in the past deflected enough cosmic radiation from the Earth to lower significantly the production-rate of carbon-14 and consequently its concentration in the atmosphere. They calculated that 2,000-yr. samples would thus give radiocarbon ages of 2,240 years. In addition, Broecker *et al.*[7], reasoning from Worthington's[8] suggestion of catastrophic overturn in the oceans, suggested that such changes in the rate of formation of deep water, if on a world-wide scale, would measurably affect the carbon-14/carbon-12 ratio in the atmosphere. If, for example, the rate of formation of bottom water were accelerated, carbon-14-depleted bottom water would reach the surface at a faster rate, reducing the carbon-14/carbon-12 ratio in the surface waters and in turn in the atmosphere. Although the results of Broecker *et al.*[7] failed to show any significant variations which might be related to non-equilibrium circulation of the oceans, DeVries[3] has recently obtained results demonstrating small oscillations (± 1 per cent) in the ratio carbon-14/carbon-12 of the atmosphere over the past few hundred years. He feels that these variations correlate well with historical climatic records in the manner predicted if the cause were variation in the rate of formation of deep water.

By applying corrections to certain published carbon-14 measurements of samples of known age, Crowe[9] has postulated that the past few thousand years have witnessed atmospheric variations over a range of 10 per cent. Munnich, Ostlund and de Vries[10] and Barker[11] have shown, however, that Crowe's corrections are unrealistic; with more reasonable assumptions, his deviations disappear.

In order to define the atmospheric carbon-14/carbon-12 ratio over historic time, a large number of samples will have to be measured from many areas and at closely spaced times. This will necessitate the co-operation of a number of laboratories. As a contribution to the problem, a number of Lamont measurements on samples of known age are reported here (summarized in Table 1). Since the results are related to the international oxalic acid carbon-14 standard distributed by the U.S. National Bureau of

Table 1. RADIOCARBON RESULTS FOR SAMPLES OF KNOWN AGE

Absolute age (yr. before 1958)	Calendar date	Method of absolute dating	Place of growth	Type of material	δ ¹⁴C	δ ¹³C	Δ¹⁴C	Carbon-14 age*	Lamont No.
1879 ± 2	A.D. 79	Historical	Pompeii, Italy	Carbonized bread	+ 8 ± 5	−21·1	+ 1 ± 5	1894 ± 40	*L*-371*E*
		Mayan calendar	Guatemala	Wood		−21·8		1502 ± 60	*L*-113
1502 ± 10	A.D. 456	(Spinden correlation)			+ 9 ± 7		+ 3 ± 7		
1242 ± 10	A.D. 716	(Goodman *et al.* correlation)			−23 ± 7		−30 ± 7		
1384 ± 5	A.D. 574	Ring counting	Kings Canyon National Park, Calif.	Sequoia wood	−13 ± 7	−18·7	−26 ± 7	1606 ± 60	*L*-108*B*
886 ± 5	A.D. 1072	Ring counting	Kings Canyon, National Park, Calif.	Sequoia wood	+12 ± 7	−20·5	+ 3 ± 7	886 ± 50	*L*-108*A*
324 ± 5	A.D. 1634	Ring counting	Pacific Northwest United States	Spruce wood	+19 ± 6	−24·9	+19 ± 6	202 ± 50	*L*-353*A*
281 ± 5	A.D. 1677	Ring counting	Pacific Northwest United States	Spruce wood	+28 ± 6	−18·0	+15 ± 6	166 ± 50	*L*-353*C*
220 ± 5	A.D. 1738	Ring counting	Pacific Northwest United States	Spruce wood	+12 ± 5	−20·9	+ 4 ± 5	204 ± 40	*L*-353*E*
148 ± 5	A.D. 1810	Ring counting	Pacific Northwest United States	Spruce wood	+16 ± 5	−24·1	+15 ± 5	56 ± 40	*L*-353*B*
133 ± 5	A.D. 1825	Ring counting	Pacific Northwest United States	Spruce wood	+13 ± 5	−22·0	+ 8 ± 5	95 ± 40	*L*-353*F*
83 ± 5	A.D. 1875	Ring counting	Pacific Northwest United States	Spruce wood	0 ± 6	−21·4	− 7 ± 6	160 ± 50	*L*-353*D*
68 ± 5	A.D. 1890	Ring counting	Palisades, N.Y.	Oak wood	+ 2 ± 5	−24·0	0 ± 5	91 ± 40	*L*-314
68 ± 5	A.D. 1890	Ring counting	Palisades, N.Y.	Pine wood	− 2 ± 6	−23·0	− 6 ± 0	0 ± 50	*L*-315

Δ^{14}C average = +3 (excluding *L*-113). Standard deviation = 17

* Ages are computed using the average Δ^{14}C as the control value.

Standards, they can be compared directly with those obtained at other laboratories.

The results are expressed in terms of Δ^{14}C, defined as follows:

$$\Delta^{14}\text{C} = \delta^{14}\text{C} - 2\delta^{13}\text{C}\left(1 + \frac{\delta^{14}\text{C}}{1{,}000}\right) - 50{\cdot}0$$

where

$$\delta^{14}\text{C} = \left\{\frac{A^{*}(\text{sample}) - 0{\cdot}950A^{0}(\text{oxalic acid})}{0{\cdot}950A^{0}(\text{oxalic acid})}\right\} \times 1{,}000$$

and

$$\delta^{13}\text{C} = \left\{\frac{R\,(\text{sample}) - R(\text{belemnite standard})}{R(\text{belemnite standard})}\right\} \times 1{,}000$$

Symbols used are defined as follows: δ^{14}C and δ^{13}C = per mille (not per cent) differences from arbitrary standards (consequently, Δ^{14}C is in per mille); A^{*} = carbon-14 activity of the sample corrected for radioactive decay between formation and measurement of sample; A^{0} = carbon-14 activity of the standard corrected for decay between January 1, 1958, and the time of the measurement; R = ratio carbon-13/carbon-12 as determined on a mass spectrometer. The constants − 50·0 and 0·950 are introduced so that the values for Δ^{14}C and δ^{14}C for pre-1900 woods (the usual modern control standards of radiocarbon laboratories) fall close to zero on the scale. (A more complete discussion of the scale used in this communication will be published in the first radiocarbon supplement of the *Americal Journal of Science* (1959).) By introducing δ^{13}C, a term based on the stable isotope ratio carbon-13/carbon-12 of the gas used for the radioactivity assay, the term δ^{14}C is corrected for isotope fractionation during the photosynthetic processes and/or during the laboratory preparation of the sample gas. Thus, if the ratio carbon-14/carbon-12 for the atmosphere is geographically uniform and has remained constant in the past, as at present assumed in dating, the Δ^{14}C values of all historically dated terrestrial plant materials should be the same within the experimental error.

The Δ^{14}C results of measurements on twelve samples which are dated historically or by tree-rings are listed in Table 1, as well as plotted in Fig. 1. Before examining the results for the purpose of drawing conclusions, it would be well to consider how the absolute ages of the samples were obtained.

Two samples, Pompeiian bread and Mayan lintel wood, are dated historically. The bread remains found at Pompeii were certainly charred in the great ash fall of A.D. 79, so that the age of the wheat is 1,879 years plus the period of grain storage; the latter is probably less than two or three years and thus negligible. In the case of the lintel wood, the absolute age is obtained from the Mayan date of 9.15.0.0.0 carved on the lintel; according to the Spinden correlation of the Mayan and Christian calendars, the date is equivalent to August 30, 481. Thus, the age of the wood is 1,477 years plus the period between growth and cutting of the tree, estimated from ring counts to be about 25 years (that is, 1,502 years). On the other hand, if the Goodman–Martinez–Thompson correlation is correct, the age is 260 years less (that is, 1,242 years).

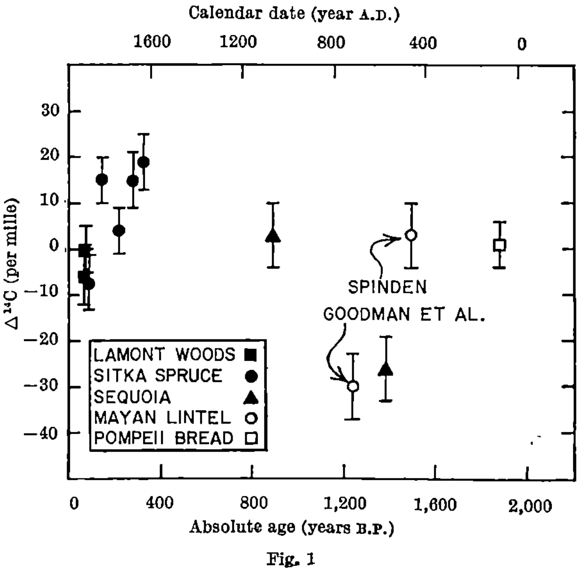

Fig. 1

The other ten samples all involve tree rings representing four individual trees, sequoia, sitka spruce, oak and pine. In all cases, the ages were obtained from the dates of cutting together with ring counts. The sequoia and spruce sections are part of the forestry collection of the American Museum of Natural History in New York City, while the oak and pine trees were obtained from the grounds of the Lamont Geological Observatory. We wish to acknowledge the aid of J. McCormack and F. Scherer, of the Museum staff, in obtaining the sitka spruce samples.

The results show a spread of ± 25 per mille about a mean of + 3 per mille. Since the standard deviation of the results is 17 per mille, in contrast to the measurement error of about 6 per mille, there is little doubt that the results include real differences. As yet it is not certain whether these results reflect world-wide or merely local variations. The three samples of highest activity (spruce woods with ages of 148, 281 and 324 years) are consistent with results obtained by both Munnich[2] and de Vries[3], pointing to a 10–20 per mille higher atmospheric carbon-14/carbon-12 ratio during the period A.D. 1630–1830. On the other hand, the 886-year-old sequoia sample and the Pompeiian bread (A.D. 79) fall close to the average and to wood grown within the last half of the nineteenth century. The results of Munnich[2] and de Vries[3] also provide support for the similarity between the atmospheric carbon-14/carbon-12 ratio of the mid- to late-nineteenth century and the late first century A.D., suggesting a difference no greater than 10 per mille. Unless further radiocarbon results fail to support this similarity, the postulated linear decrease of the Earth's magnetic field suggested by Thellier's[5] residual magnetism data is improbable. Whether the low value represented by the 1,400-year-old sequoia sample is truly representative of a world-wide condition is uncertain. If it is, then the calendar correlation of Goodman *et al.* gains support. But if the average of all samples is more typical of the Mayan atmosphere, the Spinden correlation is favoured.

From the above discussion, it should be clear that more observations on samples of known age are needed to increase the accuracy of radiocarbon dates on recent samples. The job is two-fold : (1) archæologists must be on the alert for accurately dated historical samples (± 10 years) and (2) radiocarbon laboratories must continually increase their counting precision well below the 1 per cent level, an average for the magnitude of variations sought here. With the present observations it can only be said that the radiocarbon age of an atmospherically derived sample younger than 2,000 years will almost always lie within 250 years of the true age.

We gratefully acknowledge the encouragement of Dr. J. L. Kulp in the work reported here. Thanks are also due to James Hubbard and Marylou Zickl for their aid in preparing and measuring the reported samples and to Glen Erickson and Roland Kologrivov for the mass spectrometric measurements of carbon-13/carbon-12 ratios.

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REFRACTION OF EXTRA-TERRESTRIAL RADIO WAVES IN THE IONOSPHERE

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SEVERAL authors, most recently Chvojkova[1], have derived approximate expressions for the refraction of extra-terrestrial radio waves passing through the ionosphere ; all have assumed a radially symmetrical ionospheric model. However, Smith[2] has shown that the diurnal variation of electron density, especially near sunrise, produces east–west horizontal gradients which result in appreciable changes in the apparent right ascensions of discrete sources. Also, recent work[3] at Sydney has shown that north–south gradients are just as important, and it is clear that an adequate treatment of the refraction problem must take account of departures from spherical symmetry.

For galactic observations at low frequencies, it is essential that some means of estimating the ionospheric refraction should be available, and one of us (M. M. K., in preparation) has derived new expressions for refraction, taking into account the effects of horizontal gradients in electron density and considering the magnitude of the uncertainties involved in the necessary approximations. The analysis has been restricted to the case of a transit radio telescope. Before including the effects of horizontal gradients, that is in the limiting case of a spherically symmetrical ionosphere, it is shown that a source the apparent declination of which is δ' is actually displaced from its true declination by $\Delta(\delta)_s$, where :

$$\Delta(\delta)_s = \sin^{-1}\left[\frac{r_m}{r_b}\sin I_b\right] - I_b - \sin^{-1}\left[\frac{r_m}{r_a}\sin I_a\right] + I_a - \sin^{-1}\left[\frac{r_m}{r_b}\sin(\delta' - \varphi)\right] + \sin^{-1}\left[\frac{r_m}{r_a}\sin(\delta' - \varphi)\right] \quad (1)$$

and the angles I_a, I_b are given by

$$\tan I_a = \frac{\tan(\delta' - \varphi)}{r_a - r_m}\int_{r_m}^{r_a}\frac{dr}{\mu_{f\cos(\delta' - \varphi)}}$$

$$\tan I_b = \frac{\tan(\delta' - \varphi)}{r_m - r_b}\int_{r_b}^{r_m}\frac{dr}{\mu_{f\cos(\delta' - \varphi)}}$$

Here $\mu_{f\cos(\delta' - \varphi)}$ is the refractive index, at a point on the ray with geocentric distance r, for a frequency $f\cos(\delta' - \varphi)$, f being the observing frequency and φ the observer's latitude. r_a and r_b are the radii of the upper and lower 'boundaries' of the ionosphere (that is, 95 per cent of the electrons are in the range $r_b < r < r_a$) and r_m is the radius of the layer of maximum electron density. Provided $(r_a - r_b) < 0{\cdot}1r_m$, the error in equation (1) does not exceed about 10 per cent.

Departures from spherical symmetry lead to extra displacements, in right ascension as well as in declination, proportional to the longitudinal and latitudinal gradients in electron density. If the shape of the layer is everywhere the same, the displacements are proportional to the gradient in f_c^2, f_c being the critical frequency of the layer. Provided the 'effective ionospheric thickness' d, defined in terms of the total electron content by $\int N\,\mathrm{d}r = d.N_{\text{max.}}$, is constant and also that the gradients $(\partial f_c^2/\partial\varphi)$, $(\partial f_c^2/\mathrm{d}L)$ are unidirectional throughout the ray path, then for moderate zenith angles the total change of declination, $\Delta(\delta)$, is given by:

$$\Delta(\delta)\cos^2(\delta'-\varphi) = \frac{d}{2r_b f^2}\left[f_c^2\tan(\delta'-\varphi) - \frac{\partial f_c^2}{\partial\varphi}\right] = d.\rho(\delta) \qquad (2)$$

and the change of right ascension, $\Delta(\alpha)$, by:

$$\Delta(\alpha)\cos\delta'.\cos\varphi.\cos(\delta'-\varphi) = \frac{d}{2r_b f^2}\cdot\frac{\partial f_c^2}{\partial L} = d.\rho(\alpha). \qquad (3)$$

The first term in $\rho(\delta)$ is an approximation from equation (1), and, in the special case defined by $\delta f_c^2/\partial\varphi = 0$, equation (2) reduces to Chvojkova's equation. It is seen that the refraction is proportional to d and hence to the total electron content, so that refraction observations give a new method of estimating this quantity.

Using the Sydney 19·7 Mc./s. Mills cross, many observations of the apparent positions of some of the stronger discrete sources have been made, and the observed refraction has been correlated with ionospheric data from the chain of ionospheric stations, along the east coast of Australia, controlled by the Australian Ionospheric Prediction Service. Values of f_c^2 and its latitudinal gradient were estimated from the simultaneous hourly values of $f0F2$ from the different stations, while the longitudinal gradient was estimated from the time variation. The results of observations of apparent declination of the sources 03*S*3*A*, 09*S*1*A* and 12*N*1*A*, made between September 1957 and May 1958, are presented graphically in Fig. 1.

There is good correlation between $\Delta(\delta).\cos^2(\delta' - \varphi)$, the refraction observed for each source reduced to a common scale, and $\rho(\delta)$ (see equation 1); we infer that for all these observations d was approximately equal to 550 km. An independent estimate obtained from the right ascension data (not shown) was 450 km., but in this case the scatter of the points was much greater. For both right ascension and declination a considerable part of the scatter is due to the uncertainties involved in interpolating from the hourly ionospheric data to the circumstances of each observation. In this connexion, the effects of large ionospheric irregularities (order of 100 km.) could be serious; short-period scintillations (order of 1 min.) have been eliminated by an averaging process in the reduction of the observations.

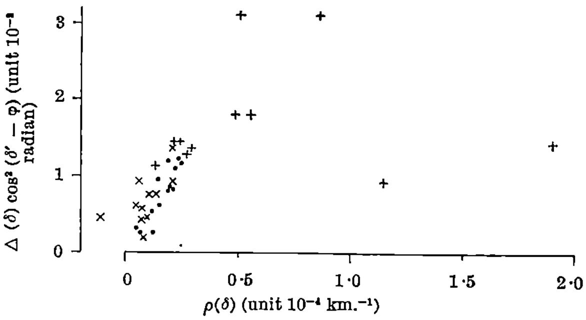

Fig. 1. Refraction under different ionospheric conditions; the quantities plotted are defined in the text. Observations of three discrete sources are indicated separately: ●, 03*S*3*A*; +, 09*S*1*A*; ×, 12*N*1*A*

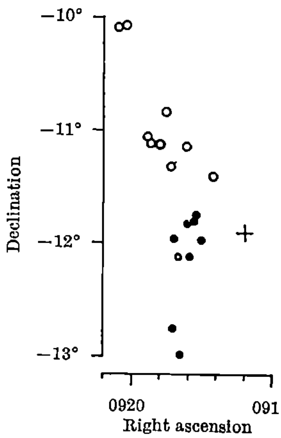

Fig. 2. 19·7 Mc./s. positions of the source 09*S*1*A*. Observed positions are shown by circles and the positions obtained after applying corrections for ionospheric refraction are shown by dots. The cross indicates the 85·5 Mc./s. position of the source

The constancy of the value of d implies that, for these observations, the total electron content of the ionosphere was directly proportional to $(f0F2)^2$.

Evans[4] has published values of the total electron content derived from observations of moon echoes at Jodrell Bank. We have estimated the total electron content to be expected at the time of his observations, assuming the constant value of d = 500 km. deduced from our refraction measurements, and taking $f0F2$ from the Slough data. There is generally good agreement with his observational results, especially in view of the differences in place and time.

As an indication of the astronomical value of the ionospheric refraction corrections, the observed and corrected positions of 09*S*1*A* are shown in Fig. 2. In declination, the scatter has been much reduced and the corrected positions, with two exceptions, are within a few minutes of arc of the 85·5 Mc./s. position[5], after corrections of about 1°. The two exceptional observations are those showing very large refraction and they have obviously been over-corrected; this is probably due to the effects of ionospheric irregularities. In right ascension the scatter is reduced, but there is a systematic shift from the 85·5 Mc./s. position; similar shifts have also been found in the observations of 03*S*3*A* and 12*N*1*A*. Since we believe that any aerial collimation error is much smaller than this, the results suggest that there were large density gradients (density increasing to the east) in the *F*-region which were not reflected in $f0F2$. These gradients must have occurred above the level of maximum ionization density, and were presumably associated with the early morning conditions under which most of the observations were taken.

A more detailed account of these and other experimental results is being prepared for publication.

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LETTERS TO THE EDITORS

GENETICS

Salmonella–Escherichia Hybrids

UNTIL recently, genetical studies with *Salmonella typhimurium* have been carried out mainly by the transduction method. In an effort to facilitate such studies, we attempted to develop a means of applying conjugation techniques also, using *S. typhimurium* and *Escherichia coli*, since Baron and his collaborators[1] had been able to produce hybrids between these two bacteria. We have been successful in experiments with a *Salmonella* culture carrying a mutator gene (*mut*) and a culture of *E. coli* strain *K*-12 carrying the factor for high frequency of recombination (*Hfr*). The mutator strain was isolated by Miyake[2] from strain *LT*-7. Its main characteristic is a 10- to 100-fold increase in spontaneous mutability.

Our procedure for the detection of recombinants is as follows. Equal volumes of over-night broth cultures of the *S. typhimurium mut* strain and *E. coli Hfr* are mixed; 0·1-ml. samples of the mixture are plated immediately on appropriate medium; and the plates are incubated for 24–36 hr. at 37° C. Under these conditions the frequency of recombinants is about 1 per 10^6 plated bacteria. Thus it is considerably lower than the frequency observed in recombination between two strains of *E. coli*.

Two *E. coli* strains have been used so far: *HfrCS*101 and *HfrC*. With the first we obtained hybrids in which the following *S. typhimurium* mutant genes were replaced by their wild-type alleles from the *E. coli* genome: ability to ferment lactose (*lac*); requirements for leucine (*leu*), arginine (*arg*), threonine (*thr*), aspartic acid (*asa*), thiamine (*thi*), proline (*pro*), glutamic acid (*glt*) and pantothenate (*pan*). With *HfrC* we have obtained hybrids incorporating the *lac, pro, leu* and *thr* wild-type alleles.

Thus it appears likely that the hybrids may carry any region of chromosome of the donor bacterium.

The results so far can be summarized as follows:

(1) Hybrids have been obtained which combine certain genetic markers carried separately by the two parent bacterial strains.

(2) Among these hybrids three types have been recognized: (*a*) sensitive to virulent *Salmonella* phage *H*5, but resistant to *E. coli* phage *T*6; agglutinated by *Salmonella* serum; (*b*) resistant to phages *H*5 and *T*6; very slight or no agglutination by *Salmonella* serum; (*c*) resistant to phage *H*5, but sensitive to *T*6; not agglutinated by *Salmonella* serum.

(3) Temperate *Salmonella* phage (*PLT*-22 *H*1) grown on a type-(*a*) hybrid will transduce markers carried in the *Salmonella* part of the chromosomal complex, provided the recipient *Salmonella* bacteria have the *mut* (mutator) gene.

(4) This same phage forms about 10^1–10^2 times more plaques on hybrid-(*a*) bacteria than on *LT*-7 bacteria carrying the *mut* gene, and 10^2–10^4 times more plaques than on *LT*-7 bacteria without *mut*. Adsorption tests indicate no difference between hybrid *LT*-7 *mut* and *LT*-7 mut^+ bacteria with regard to phage adsorption.

(5) The approximate order of certain loci in the *Salmonella* genome as determined by these recombination tests is: *mut—thr—leu—pan—pro—lac*. There is evidence that *pro* and *lac* are close together and close also to *asa, glt* and *arg*.

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A Further Example of the Kell Blood Group Phenotype K−,k−,Kp(a−b−)

IN an earlier communication[1], we reported two sisters having the Kell phenotype K−,k−,Kp(a−b−). The parents were second cousins, and it was assumed that the sisters were homozygous for a Kell gene the product of which does not react with any of the known Kell antisera. Allen *et al.*[2] later gave this gene the abbreviation K^0. Alternatively, there may be a deletion or suppression. We have sought for other examples of this phenotype by using the serum of the propositus of the above family by the capillary–papain method[3]; by this method the serum reacts with all K+ or k+ bloods. The 3,122nd blood so tested did not react, indicating that it was of the phenotype we sought. This was confirmed by testing with anti-K, anti-k, anti-Kp^a and anti-kp^b; it reacted with none of these.

The parents of the propositus, Mrs. Kan, are first cousins. Her husband, two children, daughter-in-law and four grandchildren are all K−,k+,Kp(a−b+). While the two children are presumably of genotype $kKp^b.K^0$, titration with anti-k and with anti-Kp^b failed to differentiate between assumed genotypes $kKp^b.kKp^b$ and $kKp^b.K^0$. The family is of Finnish descent. The mother and six brothers and sisters of the propositus live in Finland.

It may or may not be significant that two members of the original family in which K^0 occurred, and two of the nine members examined in the present sibship, had suffered abnormal bleeding for which they were transfused; further, the new-born baby of the propositus in the first family suffered from a form of erythroblastosis fœtalis in which petechial hæmorrhages of the skin were a prominent sign.

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BIOLOGY

The River Niger as a Barrier in the Spread Eastwards of Hæmoglobin C : a Survey of Hæmoglobins in the Ibo

HÆMOGLOBIN C is associated with West Africa rather than with Africa as a whole. It differs in that respect from hæmoglobin S, which is distributed throughout that continent south of the Sahara and north of the River Zambezi. Within West Africa the highest incidences are found in northern Ghana, where Dagomba, Moshie and Dagarti were seen to include 28, 22, and 16·5 per cent, respectively, of people with hæmoglobin C (ref. 1). Similar high incidences were found in the French territories bordering northern Ghana[2]. East of Ghana hæmoglobin C is still found at an appreciable incidence as far as Western Nigeria in the Yoruba. Thus Allison[3] saw hæmoglobin C in 6 per cent of 104 Yoruba resident in Ghana, and Walters and Lehmann[4] in 7 per cent of 940 inhabitants of a Yoruba village 40 miles north-east of Lagos. Garlick and Barnicot[5] examined 305 Yoruba school-children in Ibadan and found hæmoglobin C in 6·5 per cent.

Though isolated examples of hæmoglobin C have been reported from areas farther east than western Nigeria, surveys have generally failed to show it at an appreciable incidence anywhere east of the River Niger. Walters and Lehmann[4] found no hæmoglobin C in 155 Igalla, a tribe closely related to the Yoruba but differing from them by having remained east of the River Niger in the course of the migration which carried Yoruba and Igalla first from the Sudan to the Bornu Province and later to their present homes. The difference in the genetic make-up of Yoruba and Igalla was attributed to the fact that by crossing the River Niger (Fig. 1) and by invading the coastal forest belt the Yoruba had become involved in warfare with tribes from Dahomy and Ghana to the west, and that raids and counter-raids must have resulted in interchange of captives which would have introduced hæmoglobin C into the Yoruba. The Igalla live in an area lying in the angle formed by the Niger in the west and its main tributary, the Benue, to the north. Hæmoglobin C has also been sought for in the Lake Chad area in the extreme north-east of Nigeria, when Roberts and Lehmann[6] found no hæmoglobin C in 105 Shuva, 116 Kanouri and 92 Bedduwa, but 6 carriers of hæmoglobin C trait among 104 Wakura. South of this region, Langouillon and Delas[7] failed to find hæmoglobin C in an extended survey, with one exception, where 224 Southern Cameroon Bantu included 1 carrier of the hæmoglobin C trait. In all these surveys hæmoglobin S was found at high frequency.

As it seems that hæmoglobin C falls sharply in frequency from west to east within Nigeria, it was of special interest to determine the incidence of this hæmoglobin in people east of the Yoruba, where about 7 per cent are carriers of hæmoglobin C trait. The most important eastern neighbours of the Yoruba are the Ibo, whose administrative headquarters are in Enugu in Eastern Nigeria. Though most of the Ibo live east of the River Niger, some of them are found west of the river—'the Western Ibo'. Edington and Lehmann[1] noted hæmoglobin C among the Ibo resident in Accra, and Allison[3] examined 51 Ibo resident in Ghana and found 3 carriers of hæmoglobin C trait among them. This sample, however, is small, and as the Ibo lived in Ghana it was possible that there had been some local admixture. An undoubted case of hæmoglobin C disease in an Ibo has been seen in Enugu by Nwokolo[8].

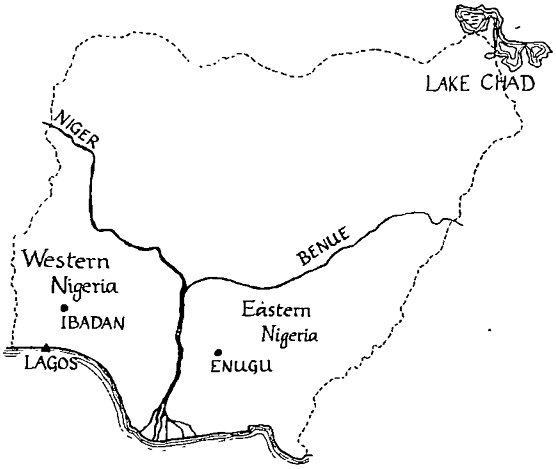

Fig. 1

We examined 257 non-related Ibo, of whom 4 came from west of the River Niger (Western Ibo) and 253 from areas in Eastern Nigeria. 36 were women-teachers attending a training college in Enugu, 17 were nurses at the Enugu General Hospital, 70 were out-patients at a leper hospital in Uzuakoli, and 134 were school-children. Of the school-children, 18 were seen in Lagos and are included in this survey by the kind permission of Dr. W. dos Santos, senior pathologist, Federal Government Medical Services, Nigeria, and the remainder at three different schools in Enugu.

The total number of school-children examined in this survey was 260, but these included non-Ibo: 108 Yoruba and the rest Ibibio, Effik and others. An interesting chance finding was the sickle-cell thalassæmia pattern (S + A + F) in one of the non-Ibo school-children examined. The child came from Benin and the family was resident in Ishan. It is of interest that Benin was exposed to a sustained Portuguese influence in the past, and the finding of thalassæmia in a child coming from Benin might indicate how the classical thalassæmia gene—which is only occasionally discovered in Africa—might have entered that continent.

Table 1. HÆMOGLOBINS IN 257 NON-RELATED IBO

Phenotype	AA	AS	AC	AG
Number	190	64	2	1

Except for the Yoruba, hæmoglobin C was only seen among the Ibo and, as Table 1 shows, there were 2 carriers of the hæmoglobin C trait among the 257 examined. The incidence of 24·9 per cent sickle-cell trait carriers among the Ibo is similar to that in the neighbouring communities of West Africa, and the finding of hæmoglobin G in one Ibo is the first example of this hæmoglobin in Eastern Nigeria. The sharp fall in the incidence of hæmoglobin C from 7 per cent in the Yoruba to less than 1 per cent farther east in the Ibo suggests that the River Niger has acted as a barrier to the spread of hæmoglobin C towards the east. The influence of that river on the distribution of hæmoglobin C is not unlike that of the river Zambezi on the distribution of hæmoglobin S.

We thank Dr. J. U. Ekpo, Enugu, and Dr. C. K. Manuel for their help with the examination of the school-children in Enugu, and Mr. E. S. Drewett for arranging the survey at the Uzuakoli Leper Settle-

ment. One of us (H. L.) would like to thank the Federal and Eastern Region Governments, Nigeria, for defraying the cost of his visit to Nigeria.

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Interaction between Ants on a Scent Trail

IT is well known that many ants lay scent trails on the ground which can be followed by other ants[1-3]. When an ant is following such a trail it is guided primarily by the scent 'marks', although other orientating factors, including visual stimuli, are sometimes also involved[2,4]. Carthy[3] has suggested that another factor contributing to the dense trails formed by *Acanthomyops fuliginosus* workers might be a tendency for workers to seek maximal contact with their companions. During a study of the trail systems of the ant *Monomorium pharaonis*[4] it was possible to record the behaviour of successive workers arriving at a branch in the trail system, and to relate this to the behaviour of the preceding ant. At such a branch each ant took either branch A or branch B, and if the proportion of all ants which took branch A was p, the proportion which took B would be $(1 - p)$. If there were no relation between the 'choice' of one ant and that of the following ant the expected proportions of pairs of successive ants taking respectively A and A, A and B, B and A and B and B would be p^2, $p(1 - p)$, $p(1 - p)$ and $(1 - p)^2$. Table 1 shows that the observed proportions conform very closely with these figures and do not differ from them significantly in a χ^2 test ($\chi^2 = 2{\cdot}02$ with 3 degrees of freedom, $P >$ 50 per cent).

Table 1. RELATION BETWEEN THE 'CHOICE' MADE BY ONE ANT BETWEEN TWO TRAILS *A* AND *B* AND THE 'CHOICE' MADE BY THE FOLLOWING ANT. FIGURES FOR ALL ANTS

Choice of first ant	*A*		*B*		Totals		
Choice of second ant	*A*	*B*	*A*	*B*	*A*	*B*	All
Observed numbers	48	63	64	58	112	121	233
Expected numbers	52·9	58·1	58·1	63·9			(233)
Contribution to χ^2	0·45	0·43	0·60	0·54			2·02

As the trails of *Monomorium pharaonis* are not very dense this result is not surprising. *M. pharaonis* were not, however, evenly distributed along the trails, but often ran close behind one another, perhaps simply because quicker ants caught up slower ones. When only such pairs of ants running almost if not quite in contact are considered, both ants of the pair took the same branch of the trail significantly more often than would have been expected if no interaction took place (Table 2, $\chi^2 = 6{\cdot}16$ with 1 degree of freedom, P lies between 1 and 2 per cent). In Table 2 different grouping of the results was necessary because of the smaller numbers involved, but the method by which the expected distribution was calculated was the same as in Table 1. As well as the sixteen pairs on which Table 2 was based there were four groups of three ants and one of seven ants, but such small numbers do not allow any conclusions to be drawn.

Table 2. RELATION BETWEEN THE 'CHOICE' MADE BY ONE ANT AND THAT OF THE FOLLOWING ANT. FIGURES ONLY FOR THOSE ANTS RUNNING IN PAIRS

	Chose the same branch	Chose different branches	Total
Observed number	13	3	16
Expected number	8·03	7·97	16
Contribution to χ^2	3·07	3·09	6·16

Apparently in *Monomorium pharaonis* one ant does tend to follow the course taken by another provided that the two are running so close together as to be almost in contact. According to Hingston[5] *Camponotus sericeus* and *C. paria* behave in a similar way. These ants, however, do not lay scent trails and the recruits reach newly discovered food by following its discoverer on the latter's return to the food from the nest. It seems possible that the trail-laying behaviour of Myrmicine ants has evolved through such a stage where one ant led another directly, and it is therefore interesting to find traces of such behaviour in *Monomorium pharaonis*.

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Mechanical Transmission of Cassava Brown Streak Virus

BROWN streak virus disease of cassava (*Manihot utilissima* Pohl.) is important in all the cassava-growing areas on the coasts of Kenya and Tanganyika, because necrosis of the starch storage tissues of the roots and stems of infected plants results in serious losses in yield[1,2]. Transmission of the virus by a white fly (*Bemisia* sp.) is suspected but has not been confirmed[3] and the only reliable means of transmitting it experimentally has been by grafting. The symptoms of the disease vary greatly with variety and environmental conditions, making diagnosis difficult, particularly when plants are infected both with brown streak and cassava mosaic, another virus disease. Thus a major difficulty in studying brown streak has so far been the lack of a means of transmitting the causal virus readily and also uncontaminated with cassava mosaic virus.

A virus causing typical brown streak symptoms in cassava seedlings has now been transmitted mechanically from cassava to several solanaceous plants. Mature leaves from infected cassava plants were macerated in water with alumina powder and 'Celite' and the extract inoculated by rubbing on the leaves of various test plants. Using this method, virus was readily transmitted to susceptible test plants, but similar extracts from young leaves gave no infections.

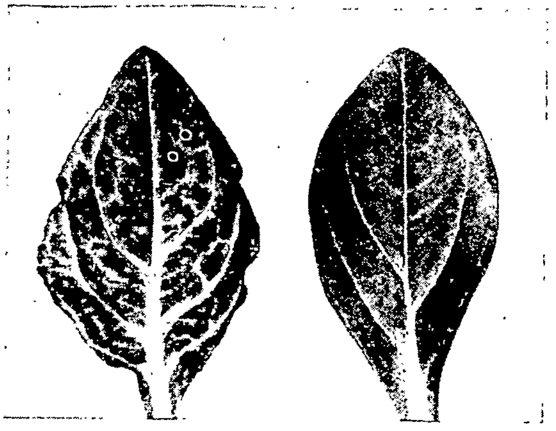

Fig. 1. Leaf of infected *Petunia* (left) with healthy leaf for comparison

Infected *Petunia hybrida* Vilm. plants were stunted and their leaves showed vein chlorosis and necrosis and were crinkled (Fig. 1). In *Datura stramonium* L. a systemic chlorosis of the fine veins developed in summer but only necrotic local lesions in inoculated leaves in winter. Inoculated tobacco (*Nicotiana tabacum* L.) leaves developed only local necrotic lesions but leaves of infected *N. rustica* L. and *N. glutinosa* L. plants showed a mild systemic vein-chlorosis. Cassava seedlings were infected by rubbing both with extracts from infected cassava and *Petunia* plants and showed symptoms consisting of a range of chlorotic patterns on the leaves similar to those described by Storey[1] and Nichols[2]. The characteristic sepia-coloured necrosis developed in the roots of some plants (Fig. 2). Though some of the cassava source-plants were infected with cassava mosaic virus, there was no indication that this was transmitted to any host by the method used.

Petunia was the most susceptible host plant found and it was used in studies on the properties of the virus. In infective *Petunia* sap cassava brown streak was rather unstable with a longevity *in vitro* of less than 24 hr. at 20° C. The infectivity of sap was drastically reduced after heating for 10 min. at 50° C. and abolished by diluting 1 : 1,000 with water. Further studies on the properties of the virus are in progress; meanwhile the development of this rapid and certain method of transmission should aid in diagnosis and in the indexing of cassava varieties for the resistance to the virus which has been reported by workers in East Africa[3,4].

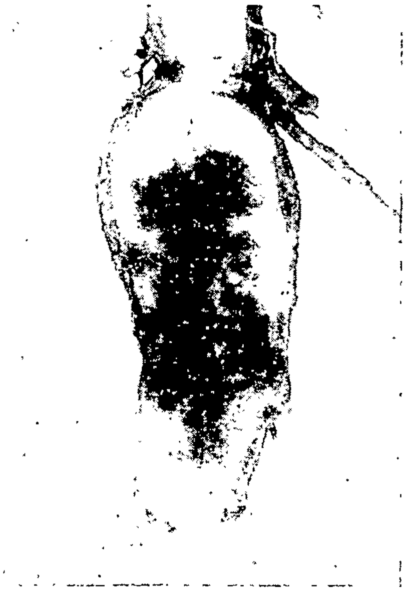

Fig. 2. Section of root of cassava seedling infected with virus from *Petunia*

Thanks are due to Mr. D. L. Jennings, now of this Institute, for obtaining the infected cassava source-plants and to Dr. H. H. Storey, of the East African Agriculture and Forestry Research Organization, for his co-operation and interest.

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Serum Transferrins

Genetically controlled variations in the β-globulins of normal human and cattle sera have recently been demonstrated by starch-gel electrophoresis[1-6]. Evidence has been presented[7] suggesting that the variable β-globulins in man are iron-binding serum proteins (transferrins). We have confirmed this directly by demonstrating with autoradiographs that iron-59 is bound specifically to the variable β-globulins in human sera, and also in cattle sera. The variable serum β-globulins in man and cattle are thus transferrins.

The results of an experiment to demonstrate the iron-binding properties of the variable serum β-globulins in humans are presented in Fig. 1. Approximately 2 μgm. of iron (containing 5 μc. iron-59) were added, as ferrous sulphate, to each ml. of serum; 0·05 ml. samples of the sera containing iron-59 (from 5 individuals) were subjected to vertical starch-gel electrophoresis[8]. The gel was cut into two slices. One slice was stained for protein (left-hand photograph in the figure); the other was used to make an autoradiograph (right-hand photograph in the figure) by placing the gel slice, wrapped in non-porous transparent film ('Saran Wrap', Dow Chemical Corporation), in contact with Kodak 'No-screen' X-ray film for 12 hr. The film was developed for 3 min. at 20° C. in Kodak formula *D*8 developer. The iron-59 is clearly bound to the variable β-globulins (indicated in the figure by white dots), which demonstrates that these proteins are transferrins. The faster migrating transferrin in each serum appears to bind relatively more iron-59 than the slower transferrin. The diffuse area of radioactivity near the sample insertion positions of some of the sera was due to the addition of more iron than could be bound by the transferrins, leading to the precipitation of inorganic iron in the gel. Addition of more serum (not containing added iron) to these samples caused the radioactivity to be confined entirely to the transferrins.

Only one transferrin (*C*) is present in the serum of the majority of individuals in all racial groups yet studied; such persons are thought to be homozygous for the genes corresponding to transferrin *C*. Two transferrins can be detected in the serum of individuals

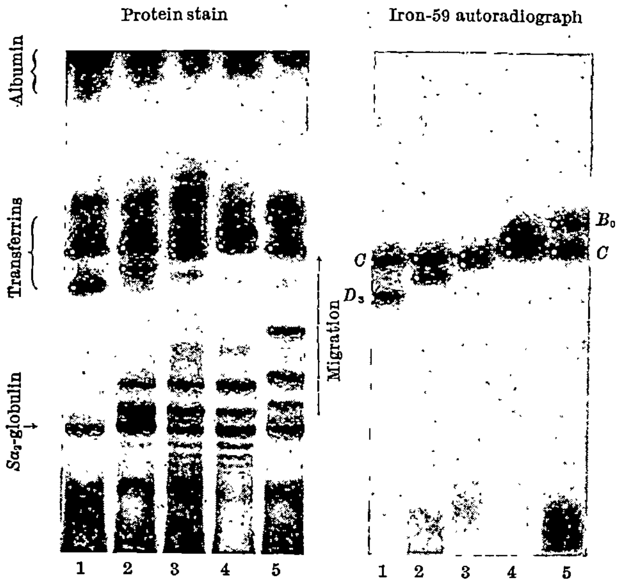

Fig. 1. The results of a vertical starch-gel electrophoresis (ref. 8) experiment with five sera containing iron-59 (plus hæmoglobin) from human individuals presumed to be heterozygous for transferrin genes. The left-hand photograph shows the protein-stained gel slice (from the sample slots to the albumin). The right-hand photograph shows the autoradiograph obtained with a second slice from the same gel. The diffuse patches of iron-59 near the sample slots are due to precipitated inorganic iron. The sera from left to right were of transferrin types (see text): 1, CD_3; 2, CD_1; 3, CD_0; 4, B_2C; 5, B_0C. The transferrin zones are indicated in the figure by white dots

who are heterozygous for transferrin genes[2-4,7]. The five sera used for the experiment illustrated were all from individuals presumed to be heterozygous for genes corresponding to transferrin C and to an additional transferrin (different in each of these five persons); three of the transferrin types illustrated (1, 3 and 5) have not been previously described:

Serum 1; *transferrin type* CD_3. Serum of this 'new' transferrin type, provisionally designated CD_3, was observed in 1 of 493 American negroes from Seattle (H. Harris, personal communication, has recently encountered a serum of the same type). Transferrin D_3 migrates in starch gels more slowly than any transferrin previously reported.

Serum 2; *transferrin type* CD_1. This serum was from an Australian aborigine. Sera of the same transferrin type, originally referred to as β-globulin type CD by Horsfall and Smithies[2], have been observed in approximately 10 per cent of Australian aborigines[2,7] and American negroes (E. R. Giblett and J. Chase, unpublished data). Comparison of a serum of transferrin type CD_1 with serum of the β-globulin type CD_1 of Harris, Robson and Siniscalco[4] indicates their equivalence. Harris *et al.* observed 3 sera of this type in 153 from Gambian negroes.

Serum 3; *transferrin type* CD_0. This 'new' type, provisionally designated CD_0, was observed in 1 of 493 sera from American negroes.

Serum 4; *transferrin type* B_2C. Serum of this transferrin type, originally referred to as β-globulin type BC by Smithies[3], has been identified with the type B_2C since reported by Harris *et al.*[4]. Sera of transferrin type B_2C were observed in 5 of 425 Canadian whites[3], and in 1 of 139 British whites[4].

Serum 5; *transferrin type* B_0C. This 'new' transferrin type was observed in 1 of 100 sera from American whites. Transferrin B_0 migrates in starch gels more rapidly than any transferrin previously observed.

Sera of two other heterozygous transferrin types (B_1C and CD_2) previously described[4] were not available at the time of this experiment. However, transferrin B_1, observed in 1 of 139 sera from British whites, migrates in the gels less rapidly than transferrin B_0 but more rapidly than transferrin B_2; transferrin D_2, observed in 1 of 153 sera from Gambian negroes, migrates less rapidly than transferrin D_1 but more rapidly than transferrin D_3 (Harris and Smithies, unpublished work). Thus 8 transferrins (B_0, B_1, B_2, C, D_0, D_1, D_2 and D_3) have now been observed in man.

It is interesting that transferrins which migrate less rapidly than transferrin C have not been reported in whites, and transferrins migrating more rapidly than transferrin C have not been observed in negroes (with the exception of one serum of transferrin type B_2C in 493 from American negroes).

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Estimation of the Size of Antigens by Gel Diffusion Methods

ANALYSIS of the pattern of precipitation lines formed when antigens and antibodies diffuse towards one another in an agar gel is established as a valuable qualitative technique in immunology. In the systems commonly used, diffusion occurs either in a tube[1] or in a flat sheet of gel[2]. Several theoretical treatments of the tube-diffusion system have been presented[3]. In the latest, and most satisfactory, by Augustin *et al.*[4], a formula is given for calculation of the approximate diffusion coefficients of antigens from accurate measurements of the position of the precipitin lines at various intervals of time. Great accuracy is not claimed for the method, however, and it is difficult to apply when several antigens are present. Korngold and van Leeuwen[5] have given a theoretical treatment for systems where diffusion occurs in a flat sheet, which enabled them to deduce that the precipitation line would be convex towards the well containing the reacting material with the greater diffusion constant. Although this conclusion is valid, the equations derived are not suitable for calculation of accurate diffusion coefficients because they depend on the assumption, which we have found to be invalid, that free diffusion continues after precipitation has begun.

Two other systems have proved satisfactory in practice.

(1) Antigen and antibody are placed in troughs cut at 90° in a uniform layer of agar on a flat glass plate. This arrangement resembles that suggested by Elek[2], who showed that in such a system precipita-

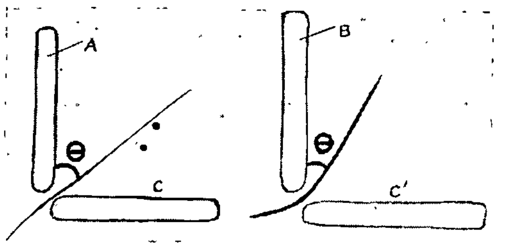

Fig. 1. Photographs of stained precipitation lines obtained by diffusion of antigen and antibody in agar gel from wells at right-angles to one another. *A*, Human serum transferrin, θ = 51°; *B*, human serum β-lipoprotein, θ = 28°; *C*, *C′* corresponding antisera

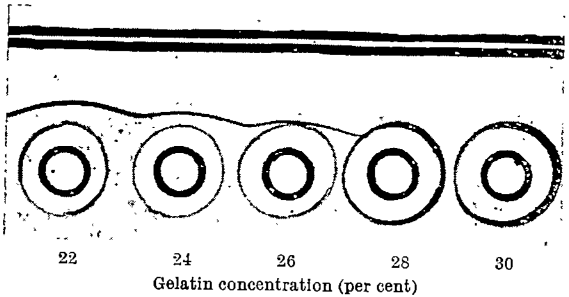

Fig. 2. Limitation of passage of human serum albumin through gelatin gels of increasing concentration

tion occurs at optimal proportions along a plane which, viewed from above, appears as a line. It can be shown that, when the amounts of antigen and antibody in the troughs are such as to give optimum proportions, precipitation will occur along a straight line inclined at an angle θ° to the antigen trough, such that $\tan\theta = (D_g/D_b)^{1/2}$, where D_g and D_b are diffusion coefficients of antigen and antibody respectively. This relationship holds true even though free diffusion is disturbed by precipitation of the reagents, but a truly straight line is formed only when the proportions of antigen and antibody in the troughs are correct. In practice, narrow straight precipitation lines are obtained within quite a wide range of relative concentrations; but when the proportions are grossly incorrect, a diffuse curved precipitate band is formed which spreads towards the trough containing the weaker reagent. Different antigen–antibody systems are precipitated independently of one another or of inert proteins present, and the diffusion coefficient of each component in a mixture can be measured, provided that the relative proportions of antigen and antibody are adjusted to be about optimal for each antigen–antibody system. Photographs of precipitate lines obtained with two representative antigens differing widely in molecular weight are shown in Fig 1. The angles of the lines are measured to within ½° on a 10 × magnified image projected on to a ground-glass screen. In Table 1 are summarized the diffusion coefficients calculated for a range of test antigens by this method, with reference to rabbit antibody, the diffusion coefficient of which was taken[5] as $3\cdot8 \times 10^{-7}$ cm.^{2} sec.$^{-1}$. The agreement with the values obtained by conventional techniques is good. These values are taken from the following sources: hen's ovalbumin, human serum albumin, human γ-globulin (Kabat, E. A., and Mayer, M. M. "Experimental Immunochemistry", C. C. Thomas, Springfield, Ill., 1948); human serum transferrin (Schultze, H. E., Heide, K., and Müller, H., *Behringwerk-Mitt.*, No. 31, 24; 1957); rat liver catalase (Price, V. E., and Greenfield, R. E., *J. Biol. Chem.*, 209, 363; 1954); sheep thyroglobulin (O'Donnell, I. J., Baldwin, R. L., and Williams, J. W., *Biochim. Biophys. Acta*, 28, 294; 1957); human serum β-lipoprotein (Levine, L., Kauffman, D. L., and Brown, R. K., *J. Exp. Med.*, 102, 105; 1955); mouse γ-globulin (Nathans, D., Fahey, J. L., and Potter, M., *J. Exp. Med.*, 108, 121; 1958, and unpublished observations); mouse urinary protein (unpublished measurements by Dr. P. C. Charlwood).

(2) An alternative technique depends upon the 'molecular sieve' properties of agar and gelatin gels, in which the size of the 'pores' or spaces within the solid phase becomes smaller as the concentration of solid increases. Polson[6] has presented evidence that penetration of proteins into agar gels is limited by their size (Table 2). We have studied agar, which forms suitable gels at concentrations of 1–7 per cent (w/v), and gelatin, which can be used at concentrations of 4–40 per cent (w/v). A convenient technique is shown in Fig. 2. A layer of 1·5 per cent agar (depth 2 mm.) is poured on a flat glass plate 10 cm. × 10 cm., and, after setting, holes are cut out with a cork borer. The holes are filled with molten gelatin or agar solutions of varying concentration (gelatin dissolved by heating in $M/15$ phosphate buffer pH 7·0 at 60°, and agar at 100°). When these plugs have set, holes with 3–4 mm. smaller diameter are cut out from the centres and sealed, leaving hollow cylinders of concentrated gelatin or agar. A narrow trough for antiserum is cut 7–8 mm. from the cylinders, and the plate is set aside for 24 hr. at room temperature for the gelatin to 'mature'. Antigen is then placed inside the cylinders and antiserum in the trough. After 1–2 days, lines of precipitate appear in the agar near those cylinders through which sufficient antigen has diffused, and lines due to common antigens fuse together. When the concentration of gel in the cylinder is high enough to prevent significant passage of antigen, no line is formed in the agar, and the line from the neighbouring cylinder appears to pass into the cylinder in question (Fig. 2). This is taken as the end-point, and is readily reproducible over a wide range of concentration of antigen and antibody. In mixtures of antigens, each reaches its end-point independently. Some results with reference antigens are given in Table 3. The technique permits estimation of the order of the effective size of antigens to within ± 30 per cent. Thus ovalbumin (mol. wt.

Table 1. DIFFUSION COEFFICIENTS (× 10^{-7} CM.^{2} SEC.$^{-1}$) OF ANTIGENS CALCULATED FROM AGAR PRECIPITATION LINES AND AS MEASURED BY OTHER TECHNIQUES

Protein	θ	Calculated D_{20}	Reported D_{20}	Molecular weight
Mouse urinary protein	58°	9·6	9·7	17,000
Hen's ovalbumin	54°	7·1	7·7	43,800
Human serum albumin	52°	6·1	6·1	70,000
Human serum transferrin	51°	5·7	5·8	88,000
Human γ-globulin	45°	3·8	3·6	177,000
Mouse γ-globulin	45°	3·8	3·9	160,000
Rat liver catalase	45°	3·8	4·1	249,000
Sheep thyroglobulin	38°	2·3	2·6	660,000
Human serum β-lipoprotein	28°	1·1	0·98	2,770,000

Table 2. PERCENTAGES (W/V) OF AGAR-LIMITING PENETRATION OF ANTIGENS

Protein	Estimated molecular weight	Concentration of agar
Caminella hæmocyanin	6,600,000	3 (ref. 6)
Human serum β-lipoprotein	2,770,000	5
Sheep thyroglobulin	660,000	7
Jasus hæmocyanin	450,000	7 (ref. 6)

Table 3. PERCENTAGES (W/V) OF GELATIN-LIMITING PENETRATION OF ANTIGENS

Protein	Estimated molecular weight	Concentration of gelatin
Human serum β-lipoprotein	2,770,000	5
Sheep thyroglobulin	660,000	7
Human and rat serum γ-globulin	177,000	18
Human serum transferrin	88,000	26
Human serum albumin	70,000	28
Hen's ovalbumin	44,000	32
Mouse urinary protein	17,000	>40

44,000) is consistently distinguished from human serum albumin (mol. wt. 70,000).

These two methods have already proved useful in estimating the size of virus antigens. Their advantage lies in the fact that values for diffusion coefficients or size of components of a mixture of antigens can be obtained at an early stage of purification. Further details and a theoretical analysis of the diffusion systems used will be submitted for publication in *Immunology*.

We are indebted to Mr. A. G. Ward, of the British Gelatin and Glue Research Association, for supplies of high-grade gelatin, and to Drs. P. G. H. Gell, T. S. Work and B. A. Askonas for gifts of β-lipoprotein, catalase and thyroglobulin, and antisera against them.

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Electron Microscopy of Synaptic Contacts on Dendrite Spines of the Cerebral Cortex

WHEN stained by the Golgi or methylene-blue method for light microscopy, certain dendrites of the cerebral cortex and elsewhere appear to have numerous spinous projections[1]. The nature of these spines has long been disputed. For example, it has been suggested that they are simply 'nutritive' expansions, or pre-synaptic end-feet, or post-synaptic processes of the dendrite—the pre-synaptic component remaining unstained[1-3]. Electron microscopy shows that the spines are in fact sites of synaptic contact.

The rat visual cortex was fixed with buffered osmium tetroxide, 'stained' with alcoholic phosphotungstic acid and embedded in araldite for sectioning[4].

Dendrites, which can be identified by their tubules[4,5], are often seen to have spinous projections. A spine (Fig. 1) is 2μ or less long and its stalk (*b*) may be as narrow as 0·1μ. The dendrite tubules (*den. t.*) are absent from the spine, which, however, frequently contains granular material. A structure, here termed the spine apparatus (*a*), often appears in the spine cytoplasm. It consists of two, three or more clear spaces (profiles of sacs, vesicles or continuous channels ?) and between each pair of opposed membranes of these 'sacs' a dense line occurs. No function can be ascribed to the spine apparatus at present. So far it has not been observed in the cytoplasm of the dendrite trunk or perikaryon.

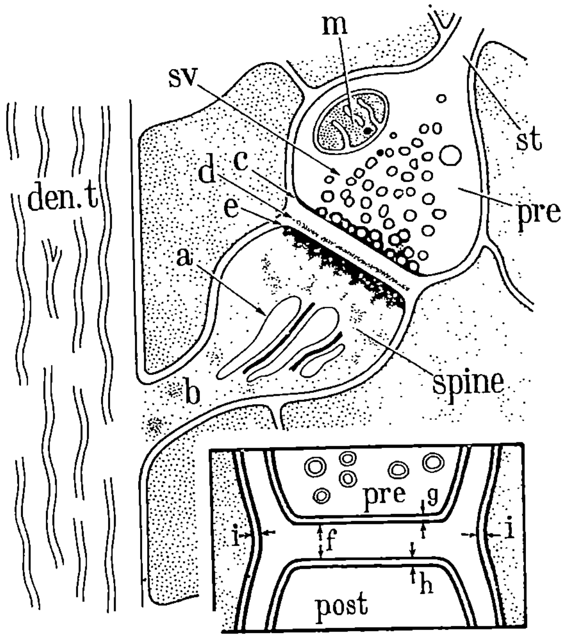

Fig. 1. Diagram of a synaptic contact on a dendritic spine, observed with the electron microscope after osmium tetroxide fixation. The stippled regions represent neuronal and glial processes of the neuropil

Inset. The opposed regions of the pre- and post-synaptic membranes seen after potassium permanganate fixation. The membranes (*i*) are of neighbouring processes of the neuropil

A pre-synaptic process (Fig. 1, *pre*) contacts the tip of the spine. The end-foot is commonly about 1μ in diameter and its stalk (*st*) (pre-terminal axon) is commonly 0·2–0·3μ in diameter. The synaptic relationship is similar to that described previously[4] for synapses formed directly with dendrite trunks. These have been termed type 1. Type 2 synapses (similar to those found elsewhere in the central nervous system) occur only on dendrite trunks and perikarya[4].

Briefly, a section of the pre-synaptic process contains usually one mitochondrion (*m*) and numerous synaptic vesicles (*sv*). Some lie in contact with the pre-synaptic membrane (*c*). Those nearest the membrane often appear denser. The pre-synaptic and post-synaptic membranes (*c* and *e*) lie 250–300 A. apart and in the extra-cellular region between them a band of electron-scattering material (*d*) occurs, sometimes slightly nearer the post- than the pre-synaptic membrane. Dense material appears associated with the cytoplasmic surface of the post-synaptic (spine) membrane (*e*). The pre-synaptic membrane (*c*), where it is opposed to the post-synaptic membrane, usually appears denser and sometimes thicker than elsewhere.

For comparison with this picture after osmium fixation the synaptic membranes have also been observed after fixation with potassium permanganate (Fig. 1, inset). Robertson[6] has described the unit membrane configuration present at cell surfaces and interpreted it in terms of organized lipid molecules. I confirm that the unit membrane structure is characteristic of cell processes of the cerebral cortex. The pre- and post-synaptic membranes (between arrows *g* and *h*) show the unit membrane consisting of two parallel dense lines, each ~ 20 A. thick, and a clear intervening layer ~ 30 A. thick. The measurement of the gap between pre- and post-synaptic processes (*f*) is consistent with the osmium picture in that the zone between the opposed pre- and post-synaptic membranes is wider than the zones between non-synaptic processes[4]. The dense band (*d*, Fig. 1) does not appear in permanganate preparations. It appears to be extracellular material and not the middle line of an external compound membrane[6], since the line occurs when the gap between membranes is closed; in this case the gap is wider than that between opposed non-synaptic processes.

In permanganate preparations (Fig. 1, inset) the dense material associated particularly with the post-synaptic membrane does not appear: nor do the synaptic vesicles nearest the pre-synaptic membrane appear denser.

The spine seen with the light microscope in suitable preparations can thus be identified with the electron microscope. The pre-synaptic end-feet, only just visible by light microscopy[7], can also readily be seen. Similar end-feet (type 1) are common on the dendrite trunks but not neuron perikarya. A full report will be published elsewhere.

I am indebted to Prof. J. Z. Young and Dr. J. D. Robertson for their interest and advice.

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Identity of the Abscission-accelerating Substance in Senescent Leaves

Van Steveninck[1], in a recent communication describing abscission-accelerators from lupins, has suggested a similarity of one of these substances to the abscission-accelerating factor discovered in senescent leaves[2], and attributes to me the statement that the latter substance is not a sugar, amino-acid, purine or pyrimidine. In fact, in the paper in question[3] it is stated that the abscission-accelerator in senescent leaves was "so far unidentified chemically, but does not appear to be any of the more common sugars, amino-acids, purines or pyrimidines".

For clearness, it might be added that using bean explants for the bioassay, and testing a wide range of concentrations, no abscission-accelerating activity has been found for glucose, fructose, sucrose, glycine, aspartic and glutamic acids, L-valine, L-histidine, L-leucine, L-tyrosine, cysteine, methionine, adenine, guanine, xanthine, hypoxanthine or uracil.

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PHYSIOLOGY

Ester Sulphate Pattern of Rabbit Bile

Isselbacher and McCarthy[1] have recently reported excretion of a sulphate conjugate of bilirubin in the bile of rats. Using paper chromatography and autoradiography of diazotized bile from rats injected with sulphate labelled with sulphur-35, they demonstrated the presence of a radioactive zone in the area of the polar azo pigment.

A series of systematic screening studies on the ester sulphate pattern of different body fluids has recently been started at our laboratory[2,3]. A brief account is given in the following of some observations made in this connexion on the occurrence of ester sulphates in rabbit bile.

Four adult rabbits with an average weight of 2·5 kgm. were used. Doses of 5–10 mc. of radioactive sulphate were injected into the marginal vein of the ear. The rabbits (which were used for other studies as well) were kept starving in metabolic cages for 24 hr. after the injection. They were then killed by insufflation of air into the ear vein. The gall-bladders were removed, the bile emptied into test-tubes, and kept in the deep-freeze unit until used.

Of the different samples of bile obtained, 5 and 25 μl. were subjected without any pretreatment to two-dimensional paper chromatography according to Datta, Dent and Harris[4]. The following solvents were used: (1) Phenol–water (400 gm. + 100 gm.). A beaker containing concentrated ammonia was placed in the chromatographic tank. (2) Butanol–2 *N* ammonia (250 ml. + 250 ml.).

After drying the papers in a stream of hot air from an electric hair-drying fan, the chromatograms were subjected to autoradiography on Gevaert 'Curix' X-ray film, exposed for one week in a wooden screw-press and developed with *G*150.

Hydrolysing experiments with hydrochloric acid and sodium hydroxide were performed on two of the samples, as follows. To 10-μl. portions of the bile in small test-tubes, 90 μl. of distilled water, 0·1 or 0·5 *N* hydrochloric acid or sodium hydroxide, respectively, were added. The tubes were sealed, and heated in a boiling water-bath for 15, 30 or 60 min. After cooling, the tubes were opened and the solutions evaporated to dryness in an exsiccator. The residues were dissolved in 10 μl. of water, and 5-μl. portions of these solutions were subjected to combined chromato-autoradiography as previously described.

A typical result of this study is presented in Fig. 1. All biles so far investigated showed the same type of pattern of radioactive spots on the autoradiograms. In addition to the occurrence of some radioactivity at the starting point of the chromatogram (1), corresponding to labelled material which did not move in either of the solvents used, and the distinct spot of inorganic sulphate (2), at least six other compounds labelled with sulphur-35 were visualized (201–206). Most of these spots were fairly resistant to alkaline hydrolysis (0·5 *N* sodium hydroxide for 60 min. at 100° C.), since only minor changes in the pattern occurred under these conditions.

Heating in hydrochloric acid, on the other hand, destroyed the whole pattern. Thus, after heating in 0·5 *N* hydrochloric acid for 15 min. at 100° C., all the 201–206 spots vanished, and a marked increase in the inorganic sulphate spot took place.

Although none of the 201–206 spots has as yet been identified, it appears that a fairly large number

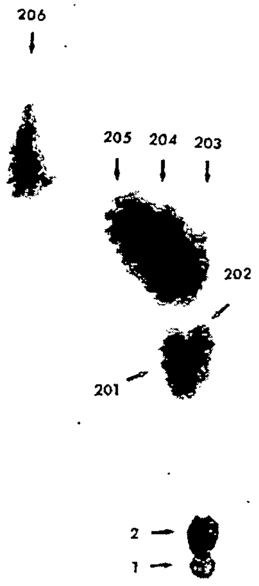

Fig. 1. Chromato-autoradiogram of 5 μl. of rabbit bile 24 hr. after injection of radioactive sulphate. Solvents: Phenol–water; butanol–ammonia. 1, Starting point; 2, inorganic sulphate; 201–203, unidentified compounds labelled with sulphur-35

of ester sulphates are excreted in the bile. Since no characteristic differences were found in this respect between the four animals studied under basic conditions, it is suggested that a characteristic, more or less constant ester sulphate pattern exists in rabbit bile.

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Site and Mode of Trehalose Biosynthesis in the Locust

THE disaccharide trehalose was first identified as an important constituent of insect hæmolymph by Wyatt and Kalf[1] using silkmoth pupæ, and it has since been found in other insect species and in nematodes[2]. Howden and Kilby[3] showed that trehalose may occur in concentrations up to 2 per cent in the hæmolymph of the desert locust, *Schistocerca gregaria* Forsk., and isolated a crystalline sample from this source. Work with the migratory locust, *Locusta migratoria*[4], and the blowfly, *Phormia regina*[5], has shown that the concentration of trehalose falls sharply during flight, and it therefore appears that this sugar is an important soluble carbohydrate and energy reserve in insects. Treherne[6] has shown that radioactive glucose introduced into the gut of *Schistocerca* rapidly gives rise to the appearance of radioactive trehalose in the hæmolymph, but nothing has been known hitherto as to the site or mode of formation of trehalose from glucose.

We have now shown that locust fat body is an important site of trehalose biosynthesis. Generally labelled D-glucose-^{14}C was incubated with fat-body tissue from *Schistocerca* (fifth instar) and the products examined by paper chromatography. A significant radioactive peak was found corresponding to the trehalose spot. Hæmolymph, leg muscle, fore, mid and hind gut tissues were also tested but found to be largely inactive in converting glucose into trehalose. The clear supernatant fraction obtained by centrifugation of an extract of homogenized and freeze-dried fat-body tissue from adult locusts was also active. After dialysis, considerable enhancement of activity was obtained by adding adenosine triphosphate (ATP) and uridine diphosphate glucose (UDPG).

Table 1

Reaction mixture	Counts per min. for trehalose spot	Counts per min. for glucose spot
Dialysed enzyme + glucose + ATP + UDPG	818	18
Dialysed enzyme + glucose + ATP	144	27
Dialysed enzyme + glucose + UDPG	324	358

Small amounts of radioactivity appeared in other peaks, but these products have not yet been identified. In another experiment, the count for the trehalose spot rose from 38 to 953 c.p.m. on adding uridine diphosphate glucose to the system containing adenosine triphosphate.

The identity of the radioactive trehalose was confirmed by the following methods. It was isolated by paper chromatography and eluted, mixed with authentic trehalose and the mixture developed on paper chromatograms using four different solvents. Radioautography of the chromatograms showed that in all cases the radioactive spots were absolutely identical in shape and position with those due to trehalose on the chromatograms, detected by Trevelyan's silver nitrate method[7]. In another experiment, the same mixture was incubated with a trehalase preparation and it was found that the rate of appearance of reducing sugar was closely paralleled by the rate of appearance of radioactive glucose and the corresponding disappearance of radioactive trehalose. The figures in Table 1 show that both adenosine triphosphate and uridine diphosphate glucose are required. In the absence of added adenosine triphosphate, considerable amounts of free glucose remain, while in the absence of uridine diphosphate glucose most of the labelled glucose is converted into products other than trehalose. Since the uridine diphosphate glucose was present in substrate amounts, the requirement for adenosine triphosphate indicates that trehalose biosynthesis occurs through phosphorylated intermediates. Cabib and Leloir[8] have shown that yeast extracts convert glucose-6-phosphate into trehalose phosphate in the presence of uridine diphosphate glucose, and it appears probable that a similar pathway may occur in insects and that the trehalose phosphate formed is hydrolysed by a phosphatase to free trehalose. This point is now being considered.

A full account of this work will be published elsewhere. We are indebted to the Anti-Locust

Research Centre for supplies of locusts and for a research studentship for one of us (D. J. C.).

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Iodine-131 Clearance-rates as an Indication of the Blood Supply of Bone

We have described[1] the use of sodium-24 clearance studies in the experimental and clinical determination of bone vascularity. Sodium-24 has a half-life of only 15·06 hr. and in the United States is only available from Oakridge National Laboratory on one day of each week. Thus it is difficult to use it for clinical investigation if more than three half-lives have transpired since its removal from the pile. This led us to search for an isotope with a longer half-life that could be used for clearance studies. Iodine-131 is readily available in most large hospitals, where it is used for the investigation and treatment of thyroid diseases. The half-life of iodine-131 being 8·0 days, it is more suitable for clinical use throughout the week than is the short-lived sodium-24.

Iodine-131 emits beta-radiation of 0·6 MeV. and gamma photons with peaks of 0·367 and 0·080 MeV. These gamma photons can be counted from the body surface and thus the clearance-rate from an injected site can be followed. Douglas and Meneeley[2] have used iodine-131 to measure the blood flow in skin flaps in plastic surgical procedures. The potential clearance of iodine-131 should be greater than that of sodium-24 as the latter must arrive at an equilibrium with the sodium of local tissue fluid; this is not a factor with iodine.

Animal experiments were undertaken to determine the suitability of iodine-131 injected as the sodium salt for clearance studies in dog femoral heads. The procedure used was the same as described previously[1]. A dose of 5 μc. iodine-131 in 0·1 ml. as sodium iodide was used and good readings obtained from the hip joints. The metal syringe previously described was used. With refinements of technique the dose of 50–100 μc. sodium-24 previously used has also been reduced to 5–6 μc. for human use. The results are shown in Fig. 1 for twenty-eight hips in 21 dogs. The same three groups of clearance values emerged as had been found with the sodium-24 clearance studies. Thirteen femoral heads were vascular with clearances of 30·9–72·9 per cent in 10 min. Ten femoral heads were completely devascularized with clearances less than 9 per cent. Two of these showed a slow rise in count of a few per cent, presumably due to diffusion of the iodine-131 through the dead femoral head, thus coming nearer to the surface of the bone during the counting period.

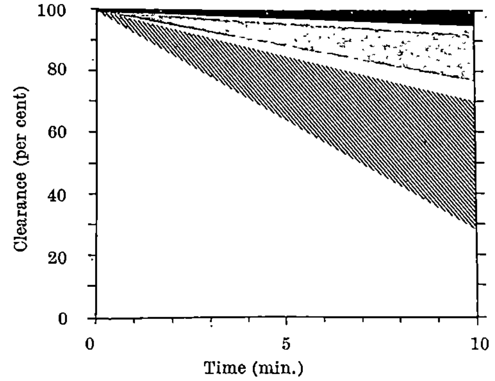

Fig. 1. Diagrammatic presentation of results on iodine-131 clearance of dog femoral heads. Black area shows avascular heads with less than 5 per cent clearance; cross-hatched area shows partially devascularized heads; and the stippled area shows the clearance in normal vascular heads

From these preliminary results there seems no objection to the use of sodium iodide-131 for the determination of the blood supply of bone in human patients. The dose of 5 μc. is small and safe and allows easy surface counting with a scintillation probe containing a 2-in. thorium-activated sodium iodide crystal. Uptake of iodine-131 by the thyroid may be prevented by pre-operative administration of iodides to the patient. Excretion of the injected sodium iodide-131 will then take place rapidly through the kidneys, thus ridding the body of the radioactive salt.

Our thanks are due to Dr. Campbell Moses, jun., under whose licence this work was performed; to Dr. Paul M. Meadows, for advice; to Mrs. Mary Grebner and Miss Patricia Orlic, for assistance; and to the U.S. Public Health Service, for grant No. 1625.

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Aqueous Humour of the Hippopotamus

The opportunity recently arose to analyse the eye fluids of the hippopotamus (*Hippopotamus amphibius*). Specimens were chosen for analysis only from animals that had been killed instantaneously, and whose ocular fluids could be removed within a couple of minutes of death. Simultaneously, arterial blood was collected anaerobically from a suitably placed bullet wound. The average volume of fluid in the anterior chamber of the eye was 1 ml.

The fluids were analysed for potassium with a flame photometer, for total carbon dioxide by Conway's microdiffusion method, for chloride by the method of Schales and Schales. Total plasma proteins were estimated by van Slyke's copper sulphate method and corrections for the total solids of the fluids were made, so as to allow the ionic constituents to be expressed as m.moles/kgm. water. The figures in Table 1 were obtained.

The figures for carbon dioxide and chloride are in keeping with those found by Davson and Luck[1] in other animals with eyes of this size and proportion. (Average weight of globe 18·0 ± 1·8 gm. (*S.E.*) average weight of lens 0·95 ± 0·05 gm., from 4 hippopotamuses). The ratios, however, for potassium in the aqueous water/potassium in plasma water are,

Table 1

Animal No.	Aqueous	Plasma	Aqueous/Plasma
Potassium concentrations (m.moles/kgm. water)			
1	5·0	11·9	0·42
2	5·4	9·0	0·60
3	5·2	8·6	0·60
4*	8·5	8·3	1·02
Total carbon dioxide concentrations (m.moles/kgm. water)			
5	34·5	36·5	0·95
6	30·7	37·9	0·81
7	27·3	37·0	0·74
Chloride concentrations (m.moles/kgm. water)			
5	116	112	1·01
6	119	107	1·11
7	128	113	1·13

* This animal's aqueous humour clotted on standing, which only occurs under abnormal conditions of aqueous humour formation, resulting in an increased permeability of the blood–aqueous barrier.

with the exception of the fourth animal in this series, quite different from those found in other species[2].

To ensure that this distribution was not attributable to artefacts in the flame photometric analysis of fluids containing protein (8·7–10·2 gm. protein/100 ml. blood in this species), aqueous humour was dialysed against plasma from the same animal; the ratio after dialysis rose to 0·97.

The further possibility that the ratio is spurious and caused by the delay between collection and centrifuging the blood in the field, with a consequent rise in plasma potassium, is made unlikely by the high concentration of potassium found in the plasmoid aqueous of animal No. 4.

The main interest in this study lies in the observed potassium distribution.

Comparative studies of plasma, aqueous humour and the cerebrospinal fluid in several mammalian species have revealed so many similarities between the ionic composition of the aqueous humour and the cerebrospinal fluid that it has been postulated that the two fluids are formed by closely similar processes[3].

The cerebrospinal fluid varies less from species to species than does the aqueous humour; this depends perhaps on the greater variety of tissues in the eye, compared with that of the central nervous system, and the species variation in the relative size of these different components.

In all mammals hitherto examined, however, there has been one consistent difference in the ionic composition of the two fluids. The cerebrospinal fluid always contains markedly less potassium than the plasma; the ratio concentration of potassium in cerebrospinal fluid water/concentration of potassium in plasma water is of the order[4] of 0·5. The equivalent ratio for the aqueous humour is nearer unity and conforms more closely to the expected ratio for a dialysate of plasma. The ionic distributions, including that of potassium in the hippopotamus's aqueous humour are similar to those of the cerebrospinal fluid in most animals and appear to lend some support to the conception that the two fluids are formed by similar mechanisms.

Why the capacity to restrict the entry of potassium into the aqueous humour should be revealed in this species is a matter for speculation. The phenomenon may, however, be related to the unusually high concentration of potassium in the plasma; it is nearly twice that of most other animals. Davson[3] has postulated that the presence of a low concentration of potassium in the fluid around nerve cells in the central nervous system serves to stabilize the neuronal resting potentials. Perhaps a similar mechanism becomes necessary also in the eye (especially the retina) in the face of an unusually high level of plasma potassium.

We wish to thank the director of the National Parks of Uganda, Mr. R. M. Bere, for permitting and assisting this study.

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Iron Content in the Serum of Cows with Hypocupræmia

Disturbances in the health of cattle accompanied by a drop in the copper-level in the blood have been observed in several countries. Sjollema[1] was the first to show that loss of appetite, anæmia, deficiency in milk output, and difficulties in breeding occurred simultaneously with a drop in the copper-level. Hypocupræmia in cattle has been found in certain areas of Poland[2]. Some investigators believe that anæmia does not occur in cases of hypocupræmia[3]. Generally, however, the metabolism of iron and of copper are believed to be interdependent[4]. Lahey *et al.*[5] noticed that the iron content in the plasma of young pigs, which were given no copper in their food, was very low. So far as I know the iron content in the serum of cows with hypocupræmia has not yet been investigated, although the hæmoglobin content has. An apparent decrease in the hæmoglobin and erythrocytes in cattle during hypocupræmia has been noticed in our studies hitherto. It must, however, be admitted that in some cases we found no anæmia.

In the present work the iron content in the serum of cows with hypocupræmia has been determined. I wished to confirm that a drop in the copper-level in the blood influences iron metabolism in cattle. It is assumed that the iron and hæmoglobin contents in the serum are a valid indicator of the iron stock in the organism.

The examinations were performed on the blood of the cattle from individual farms in the districts of Białystok and Olsztyn. In 67 of 120 animals hypocupræmia was found. Copper was determined by the method of Eden and Green[6]. Iron in the serum was determined by the standard photometric method[7]. 45 cows from the Zootechnical Institute were used as a control group. The results are shown in Table 1.

Table 1

No. of cows	Average copper content (mgm. per cent)	Range	Average iron content (mgm. per cent)	Range	Average hæmoglobin content (gm. per cent)	Range
45 (controls)	98·8	79·7–135·0	181	135–215	11·4	8·5–13·3
67	49·7	8·6 75·8	126	86–215	8·2	5·9–10·3

These results obviously indicate that iron metabolism is affected by hypocupræmia. Detailed results will be published elsewhere.

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Effect of Protein-free Diet on the Vitamin A Storage in the Rat Liver

SEVERAL workers[1-4] have reported that diets low in protein reduced the storage of vitamin A in the liver and increased the rate at which stored vitamin A was depleted. On the basis of such data, a conclusion was drawn by investigators that protein is a necessary dietary constituent for normal storage and utilization of vitamin A. The work described here was designed to test the validity of the former hypothesis by comparing hepatic vitamin A storage in young rats fed an 18 per cent casein diet and in animals fed a protein-free diet under the conditions of controlled intake of vitamin A.

Six comparable pairs of weanling albino rats of the Yale strain with an average initial weight of 50 gm. were chosen for the study. One member of each pair was fed a protein-free diet, while the other member was given an 18 per cent 'vitamin-free' casein diet for a period of 3 weeks. Each animal was kept in a separate cage and was allowed to eat and drink *ad libitum*. The basal protein-free diet was comparable in composition to that of Rechcigl, Loosli and Williams[5] with the exception of the vitamin mixture. The vitamins used in this study were supplied in the form of *GBI* B Complex Dry Mix (purchased from General Biochemicals, Inc.) supplemented with α-tocopherol and vitamin D. Vitamin A was given orally to each rat every 48 hr. in the form of vitamin A acetate at a level of 30 I.U. Following a 3-week experimental period, the animals were killed and their livers analysed for the vitamin A content by the method of Ames *et al.*[6]. As a control, vitamin A was also determined in the livers of two additional rats at the beginning of the experiment. The livers of these control animals were found to contain 14·9 and 17·1 μgm. vitamin A.

The results of the experiments are shown in Table 1. The animals which were fed a protein-free diet lost an average of 16 gm. body-weight while those fed the casein diet gained 72 gm. in a 3-week experimental period. Despite this large loss of weight, the rats kept on a protein-free ration stored just as much vitamin A in the liver as did the animals fed a ration supplemented with 18 per cent casein. In fact, the casein-fed rats stored less vitamin A than the animals kept on a protein-free diet. Thus the average liver vitamin A content of the former group was 54·7 μgm. and that of the latter 96·1 μgm. In view of the considerable difference between the liver weights of the two groups it was of interest to compare the vitamin A content when expressed per unit of weight. The casein-fed rats contained an average of 9·3 μgm. vitamin A/gm. liver whereas the rats which were kept on a regimen devoid of any protein stored 71·2 μgm./gm. liver. The lower vitamin A value in the former group can be possibly explained by greater requirement of vitamin A for the purposes of rapid growth.

Table 1. GROWTH AND LIVER VITAMIN A STORAGE OF RATS FED 18 PER CENT CASEIN DIET AND PROTEIN-FREE DIET

Pair No. and sex	Protein-free		18 per cent casein	
	Weight gain (gm./3 weeks)	Vitamin A (μgm./liver)	Weight gain (gm./3 weeks)	Vitamin A (μgm./liver)
1 ♀	−13	103·2	70	64·4
2 ♀	−13	107·0	56	54·1
3 ♂	−16	75·0	83	39·6
4 ♂	−15	91·2	71	44·0
5 ♂	−19	94·1	70	47·3
6 ♂	−20	106·3	83	35·5
Average	−16	96·1	72	54·7

These results clearly demonstrate that under the given experimental conditions the rats fed a diet lacking in protein were able to store large amounts of preformed vitamin A in their livers, suggesting that protein is not absolutely essential for this process. This finding is supported by a recent observation of Arnrich and Pederson[7] that the level of dietary protein has no effect on vitamin A storage in the liver.

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Bioassay of Sheep Anterior Pituitary Glands

A HIGHLY significant seasonal variation in frequency of twin ovulations in Merino ewes was observed by Radford[1]. In order to determine whether this was correlated with seasonal variation in pituitary gonadotrophin content the surviving ewes from Radford's experiment were later killed—16 in mid-summer (January–February 1958) and 11 in mid-winter (June–July 1958). Each ewe was killed 14 days after œstrus.

From examination of the corpora lutea present in the ovaries at slaughter it was determined that seven of the 16 ewes in January–February, and eight of the 11 ewes in June–July had shed two ova at the recorded œstrus. The pituitary glands were removed, trimmed, deep frozen immediately after slaughter, and stored at −17° C. In October 1958, each gland was homogenized with 3 ml. distilled water. 1 ml. of a buffer (sodium borate, 0·05 ionic strength; sodium chloride, 0·45 ionic strength; *p*H 8·8) was then added to each homogenate. After

Table 1. ANALYSIS OF VARIANCE. THE DEGREES OF FREEDOM (D.F.) FOR ERROR (WITHIN-GROUP VARIANCE) ARE REDUCED BY FIVE, COMPRISING ONE FOR REGRESSION OF RESPONSE ON BODY-WEIGHT AND FOUR FOR MISSING PLOTS

Source of variation	D.F.	Mean square
Slope	1	6,790*
Pituitary glands		
Between groups†	3	160
Within groups	21	358*
Interaction	24	93
Error	45	62

* $P < 0{\cdot}001$.

† Groups consisting of ewes which had shed one or two eggs at the recorded œstrus, at the two slaughter times January–February or June–July.

1½ hr. extraction they were centrifuged and the supernatants freeze-dried. All steps were carried out at 0° C. The resultant powders were dissolved, each in 1·0 ml. distilled water, and the extracts were assayed simultaneously, using the immature mouse uterine weight assay[2]. Pairs of mice were injected subcutaneously with 0·3 ml. or 0·1 ml. per mouse and killed 44 hr. later. Mouse uterine and body-weights were recorded at autopsy and the data, after log transformation, were submitted to analysis of variance using the pair totals corrected for concomitant variation due to body-weight differences (Table 1). The results for two sheep were incomplete, due to the responses at the lower level being minimal. However, the pair totals in these cases were treated as missing plots with the appropriate reduction in degrees of freedom for error.

The slopes of the log dose – log response lines were homogeneous (mean slope, $b = 34{\cdot}5 \pm 10{\cdot}8$) and the mean responses for each pituitary gland differed significantly from sheep to sheep. There were no significant differences between the mean responses of the four groups of sheep.

The following conclusions seem warranted from the results.

There were no appreciable seasonal differences in gonadotrophin content of the glands in this experiment. Indeed, the lack of any difference between ewes which had shed one or two ova at the one time of the year, and the variability between individual sheep suggest that seasonal differences would have to be large to be observed. It is not known to what extent, if any, the different periods of storage at −17° C. contributed to this result. The weights of the frozen pituitary glands or body-weights of the sheep did not contribute to the variability between sheep since the correlations between response and pituitary weight (0·06) and response and body-weight (0·11) were non-significant.

The mouse uterine weight response has been shown to give satisfactory results and should find wider application in examining individual pituitary glands for gonadotrophin content. This is important since recent work by Lamond and Claringbold[3] has shown that numerous gonadotrophins elicit similar joint action in uterine responses, thus providing a uniform basis for interpretation of pituitary–gonad studies of the type described in this communication.

There is no evidence to suggest that the yield of gonadotrophin could be much increased by a different extraction procedure. However, if this could be done it would greatly increase precision of the assays by enabling the use of a greater number of mice. A minimum of eight mice per gland would be needed to allow satisfactory potency estimates of individual glands relative to a standard and if this were achieved it would make possible comparisons between different laboratories and between different times in the same laboratory.

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Response of Rice to Small Differences in Length of Day

DORE[1] has recently reported the response of a Malayan rice, an 'indica' variety of *Oryza sativa* L., to small differences in photoperiod. I have obtained similar results with West African upland cultivated rices, varieties of *Oryza sativa* L. and *Oryza glaberrima* Steud. The latter is the main indigenous rice cultivated in Northern Nigeria. Monthly sowings (May to October) of two varieties of *O. glaberrima* in Ibadan—

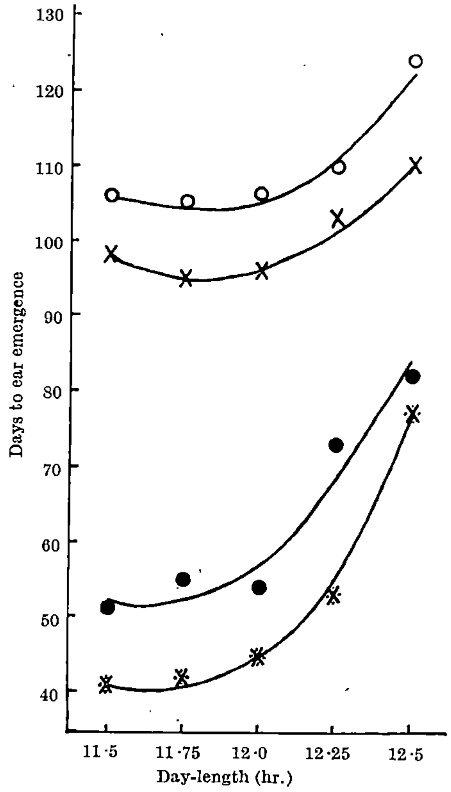

Fig. 1. Effect of small changes in photoperiod on flowering time. ○—○, *O. sativa* var. Gbengbete 223; ×—×, *O. sativa* var. Nagalawa Red Husk; ●—●, *O. glaberrima* var. Biya Gero; ✻—✻, *O. glaberrima* var. Ba Yawuri

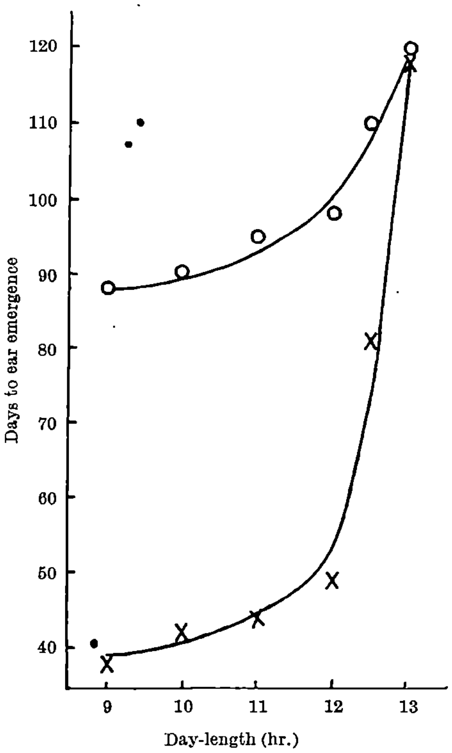

Fig. 2. Effect of photoperiod on flowering time. ○—○, *O. sativa* var. Ngalawa Red Husk ; ×—×, *O. glaberrima* var. Ba Yawuri

latitude 7° 26′ N.—showed marked variation in time to ear emergence from sowing date, the later sowings flowering earlier. The time between sunrise and sunset at Ibadan varies from 11 hr. 40 min. in December to 12 hr. 33 min. in June.

Experiments in which the plants were given constant day-lengths, controlled by time switches, of a range similar to the natural photoperiods and differing by 15 min., showed that the field behaviour could be explained by the photoperiodic response under experimental conditions. For comparison the experimental studies were extended to two varieties of *Oryza sativa* L. cultivated in Sierra Leone. Apical bud dissections carried out at regular intervals showed that the time from inflorescence initiation to emergence did not vary significantly between the day-length treatments. The day-length effect on inflorescence initiation therefore parallels that on emergence. Fig. 1 shows for four rice varieties the curvilinear relationship between the time to ear emergence and photoperiod.

The varieties of *O. glaberrima* are earlier and more sensitive than the *O. sativa* varieties, but both species show over the range of natural day-lengths a quantitative short-day response similar to that reported by Dore, although these West African rices appear to be less sensitive than the Malayan one.

From the shape of the curves shown in Fig. 1 it was expected that by decreasing the day-length below 11½ hr. the curves would rise again on the left, and it would thus be possible to define optimum photoperiods such as those reported for 'indica' varieties of *O. sativa* by Chandraratna[2]. This expectation was not fulfilled, as can be seen from Fig. 2, which gives the results of experiments with day-length treatments varying from 9 to 13 hr. There is no evidence of a lower limiting photoperiod. If there is an optimum it must be well below 9 hr., outside the range of natural day-lengths. For *O. glaberrima* var. Ba Yawuri a number of plants did not flower at the 13 hr. day-length during the period of the experiment. Thus the upper limiting photoperiod for this variety appears to be close to 13 hr.

In the experiments on the effect of small differences in day-length reported above, 15 min. differences were used because the time switches available could not measure smaller differences accurately. But it is clear from the response curves, particularly of the *O. glaberrima* varieties, that in the steep parts of the curves, day-lengths 12–12½ hr. in Fig. 1, still smaller differences in day-length would produce appreciable effects on flowering time. Previous evidence for the response of rice to small changes in day-length is provided by the work of Kuilman cited by Bünning[3]. I have reported similar responses for Nigerian plants other than rice[4]. Details of the experimental method used in the present work are as given in that paper.

I wish to thank Mr. R. Q. Craufurd of the West African Rice Research Station, Rokupr, Sierra Leone, for seeds of the varieties of *O. sativa*, and Mr. J. E. Y. Hardcastle of the Federal Rice Research Station, Badeggi, Nigeria, for seeds of the varieties of *O. glaberrima.*

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Feb. 19.

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Utilization of Alcohol in Germinating Pea Seedlings

Recent communications reporting a stimulation of growth in algae[1,2] and in seedlings[3] caused by added ethanol solutions have prompted us to report our findings of the ability of pea seedlings to oxidize alcohol which had accumulated under anaerobic conditions.

After soaking dried Kelvedon Wonder pea seeds in water at 20° C. for 20 hr., 404 mgm. alcohol/100 gm. fresh weight had accumulated. The peas were then placed in moving air on moist filter paper at 25° C. After 24 hr. the alcohol content had fallen to 270 mgm. alcohol/100 gm. fresh weight and 76 mgm. after 46 hr., by which time the radicles had emerged.

To check that the loss was not due to the volatility of the alcohol, a similar 100-gm. batch of peas was placed in a closed container through which an air-stream circulated. The outflowing gas-stream was bubbled through two absorption tubes containing concentrated sulphuric acid. When the alcohol content of the peas had fallen from 432 mgm./100 gm. fresh weight to 19 mgm./100 gm. fresh weight, only 22 mgm. of alcohol were recovered from the acid traps. A similar fall in alcohol content occurred when the peas were allowed to germinate under sterile conditions.

Acceleration of the loss of alcohol was caused by splitting or by complete removal of the seed coat. Thus cotyledons with 368 mgm. alcohol/100 gm. fresh weight contained 55 mgm. after 24 hr. at 25° C. The rate of carbon dioxide output and of oxygen uptake increased rapidly during the initial stages of the loss of alcohol, decreasing with time as the alcohol content was depleted. However, the stimulation in carbon dioxide output only accounted for the disappearance of about 25 per cent of the alcohol. The respiratory quotient during this period equalled 0·5.

Preliminary examination of extracts of the peas during germination have shown temporary increases in acetaldehyde content associated with the disappearance of the alcohol and also, as shown by paper chromatography, increases in acetic and citric acids.

In this tissue there is, therefore, evidence that alcohol accumulated under anaerobic conditions can be metabolized under aerobic conditions, and experiments are in progress to elucidate these problems further.

One of us (E. A. C.) is the holder of a research studentship awarded by the Department of Scientific and Industrial Research, for which grateful acknowledgment is made.

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Effects of Heat and Loss of Moisture on the Dormancy of Wheat, and some Interactions with 'Mergamma *D*'

A PREVIOUS communication[1] described the action of oven treatment at 38° C. in overcoming dormancy of barley without loss of moisture. Further experiments have shown that wheat does not respond in the same manner. Oven treatment in polythene appears to have no effect, and with loss of moisture the dormancy may increase.

The following results were obtained with Cappelle Desprez Wheat, ref. *A*101, approximately three weeks after harvesting (moisture content 17·5 per cent) (Table 1).

Table 1

Treatment	Control *R*°	Refrigeration	38° C. dried		38° C. polythene	
Duration of treatment	2 days	3 days	Overnight	2 days	Overnight	2 days
Germination at six days (per cent)	46	98	34	34	51	51

Peko wheat, ref. 2019, treated with mercury/BHC seed dressing ('Mergamma *D*') behaved similarly, although the seedlings showed typical signs of stunting (Table 2).

Table 2

Dormancy treatment	Peko wheat (ref. 2019)		2019 dried	
	Non-dressed	Dressed	Non-dressed	Dressed
None	83	76	86	87
Refrigeration	86	90	89	93
Oven-polythene	—	75	—	—
Oven-dried	—	67	—	73

The dried portion had been reduced from 19 per cent to 16 per cent moisture by an 'in-sack' drier before dressing. When tested, all samples had lost a further 0·5–1·0 per cent moisture.

It is evident that the reduced germination was due not only to the laboratory drying treatment, but also to some action of the dressing. This enhancing of dormancy has been suspected for some time without definite evidence (Thomson, J. R., personal communication). When tested immediately after dressing, this sample gave the following results: control, 72 per cent; dressed normal rate, 59 per cent; dressed twice normal rate, 24 per cent. Refrigeration led to maximum germination in each case, although increased dressing gave increased stunting.

Reduction in the degree of stunting of dressed wheat can result from oven treatment with or without drying. Sometimes this is manifest as a mere ⅛-in. increase in root-length. Other samples show greater response; a root-length of ¾ in. becoming 1½ in. in the treated sample, as occurred with Peko wheat 2019.

Dressed barley responds in the same manner. One sample of Proctor tested immediately after dressing produced roots of about 1 in. long, but when oven treated (in polythene) the roots were so similar to the non-dressed control that the differences would not have noticed in routine testing. Such a strong response has not yet been noticed with any wheat samples.

These observations may be of increasing interest in view of the suggestion that seed be tested for germination under the Seeds Act after the application of dressings[2].

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Effect of Pyrimidine Deoxyribonucleotides on the Regeneration of Bone-Marrow in Irradiated Mice

THE effect of several nucleotides and nucleosides on the survival and peripheral blood-count of irradiated mice was studied in our previous experiments[1]. The subject of this communication is the mitotic index in bone-marrow and deoxyribonucleic acid synthesis in the spleen in mice after irradiation and administration of pyrimidine deoxyribonucleotides.

Female mice of strain *H*, weighing 20–25 gm., were subjected to total-body irradiation at a dose of 500 r.; 0·1 mgm./25 gm. body-weight deoxycytidylic acid and 2 mgm./25 gm. thymidylic acid as the calcium salt were injected 24 hr. after irradiation. The corresponding nucleosides were injected in equimolar concentration. The mitotic index was determined before irradiation and on the fourth, seventh and tenth days thereafter; six animals of each group were used at each interval and three such experiments were performed with both cytidine and thymidine derivatives. The bone-marrow was stained by the Feulgen method and 5,000–10,000 nucleated cells were counted from the femur of each animal. The rate of deoxyribonucleic acid synthesis was determined 2 hr. after injection of phosphate-32. The deoxyribonucleic acid phosphorus from the spleen was isolated by Schmidt and Tannhauser's method.

Both deoxyribonucleotides in the given amount stimulated the regeneration of bone marrow in irradiated animals. The results were statistically significant on the fourth and seventh days after irradiation. On the tenth day and after injection of nucleosides, the differences were no longer significant. In Fig. 1 the effect of thymidine and thymidylic acid is shown, the mean value before irradiation being taken as 100 per cent. This corresponds to 11·3 mitoses/1,000 nucleated cells.

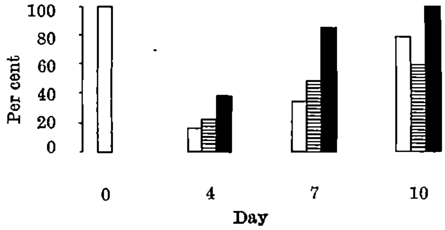

Fig. 1. The mitotic index in mice bone-marrow on the fourth, seventh and tenth day after irradiation and injection of saline (white); 2 mgm. calcium thymidylate (black); and 1·25 mgm. thymidine (shaded)

The number of chromosomal aberrations was somewhat higher in animals treated with deoxyribonucleotides than in the control group (on the fourth day 12 per cent compared with 11 per cent, on the seventh day 10 per cent and 5 per cent) but the differences were not statistically significant. In similar experiments with unirradiated mice the mitotic index was not influenced.

The changes in deoxyribonucleic acid synthesis were in the same sense as the changes in the mitotic index in bone-marrow. Results obtained on the seventh day after irradiation in mice injected with deoxycytidylic acid and deoxycytidine are given in Fig. 2.

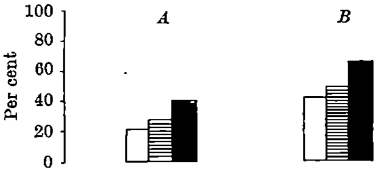

Fig. 2. The mitotic index in bone-marrow (*B*) and the rate of deoxyribonucleic acid synthesis in spleen (*A*) on the seventh day after irradiation and injection of saline (white); 0·1 mgm. deoxycytidylic acid (black); or 0·075 mgm. deoxycytidine (shaded)

The results thus agree with those arrived at in previous studies of the peripheral blood count. They show that pyrimidine deoxyribonucleotides hasten the regeneration of hæmatopoietic tissue after irradiation.

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Mixed Pigments in Colour Vision

Rushton[1] has recently suggested that the 'red' mechanism of the normal eye depends upon a mixture of two light-sensitive pigments, one of which is the same as that used for the 'green' mechanism. Marriage[2] has pointed out that addition of 'green' sensitivity to the red mechanism in this way will not affect the position on the chromaticity diagram of the red fundamental stimulus, but will affect that of the green fundamental stimulus, and will move it towards or away from the red fundamental point.

It is interesting to observe, therefore, that while the red and blue fundamental points have been determined by a number of different workers to a fair degree of consistency, efforts to locate the green point have always shown considerable scatter in the red–green direction; indeed, while some locations are at the green end of the diagram[3] others are in the opposite direction in the region well beyond the red end of the diagram[4]; and, while this abrupt difference is an artefact of the diagram itself, there is none the less a very considerable scatter.

It seems possible, then, that this scatter, which has for so long confounded efforts to locate the green fundamental point, may be caused in large part by variations in the relative amounts of the two pigments present in the red mechanism of the eye, the proportions of which could depend in various ways on the viewing conditions.

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Kodak, Ltd.,
Wealdstone, Middlesex.
Harrow, Feb. 2.

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BIOCHEMISTRY

Native Tobacco Mosaic Virus Protein of Molecular Weight 18,000

X-ray diffraction data on tobacco mosaic virus have been interpreted in terms of protein repeat units with a molecular weight of about 18,000 arranged in a helix[1]. Amino-acid analyses and end-group titrations[2] yield a similar minimal value but do not answer the question whether the ultimate molecular weight is 18,000 or some integral multiple of it. Thus far, the smallest native protein particles obtained by degradation of tobacco mosaic virus[3-5] have shown molecular weights of about 100,000. We have now been able to dissociate tobacco mosaic virus protein into undenatured particles with a sedimentation coefficient consistent with a molecular weight of 18,000.

Sedimentation studies were carried out in the synthetic boundary cell in a 'Spinco' ultracentrifuge at temperatures of 0–6° C. on protein prepared by treatment of tobacco mosaic virus at *p*H 10·3 and afterwards diluted to concentrations as low as 0·01 per cent with 0·05μ phosphate buffer at *p*H 7, with 0·1μ phosphate buffer at *p*H 6·5 or with 0·1μ borate buffer at *p*H 9. The centrifuge was operated at 59,780 r.p.m. and the boundary migration was followed by schlieren optics. As can be seen in Fig. 1, when the protein is diluted, the sedimentation-rate decreases from the value of about 4 Svedbergs frequently observed. The minimum value was 1·9

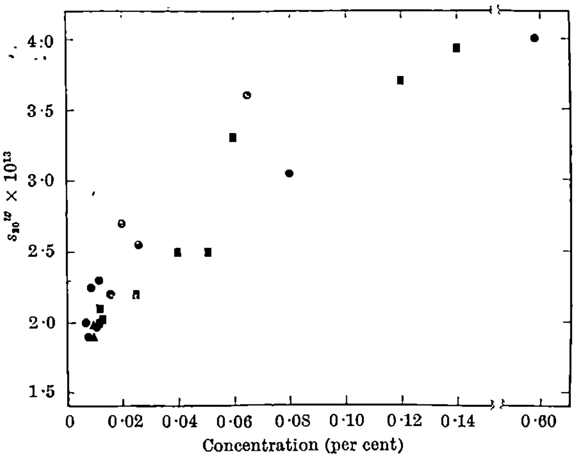

Fig. 1. Sedimentation coefficients of tobacco mosaic virus protein at various concentrations. ●, 0·10μ borate buffer, *p*H 9·0; ▲, 0·05μ phosphate buffer, *p*H 7·0; ■, 0·10μ phosphate buffer, *p*H 6·5

svedbergs. Control experiments were performed on Southern bean mosaic virus nucleoprotein diluted to the same low concentrations. Sedimentation coefficients agreed well with values extrapolated from determinations made at higher concentrations, thereby demonstrating that reliable measurements can be obtained by the method used.

If the X-ray diffraction data on the nucleoprotein of tobacco mosaic virus have been interpreted correctly, then the ultimate particle of the virus must be a truncated wedge with a maximum dimension or length of 70 A., with a thickness of 23 A. and with a maximum width of 34·8 A. It is virtually certain that the coefficient of friction lies between those of two elongated ellipsoids of revolution, both with semi-major axis of 70/2 A. and one with a semi-minor axis of 23/2 A. and the other with a semi-minor axis of 34·8/2 A. This type of reasoning, introduced by Lauffer and Szent-Györgyi[6], proved successful in interpreting the sedimentation behaviour of myosin and myosin fragments. The translational coefficient of friction, *f*, for randomly oriented elongated ellipsoids of revolution is given by the equation:

$$f = \frac{6\pi\eta b \sqrt{(1 - a^2/b^2)}}{\ln\left(\frac{1 + \sqrt{(1 - a^2/b^2)}}{a/b}\right)}$$

where η is the coefficient of viscosity, b is the semi-major axis and a is the semi-minor axis. The coefficients of friction in a medium having the viscosity of water at 20° C. for the smaller and for the larger ellipsoid are $3{\cdot}49 \times 10^{-8}$ and $4{\cdot}52 \times 10^{-8}$ C.G.S. units, respectively. By using the sedimentation formula:

$$s = \frac{M\,(1 - V\rho)}{Nf}$$

where s is the sedimentation coefficient corrected to water at 20° C., M is the molecular weight, N is Avogadro's number, V is the partial specific volume and ρ is the density of the medium, one can calculate the range of molecular weights consistent with a sedimentation coefficient of $1{\cdot}9 \times 10^{-13}$ C.G.S. units. The value of V was taken[4] to be 0·74 ml./gm. Molecular weights of 15,000 and 20,000 were obtained with the higher and with the lower friction coefficient, respectively. Since these values bracket 18,000, the sedimentation coefficient of 1·9 Svedbergs is concordant with the protein repeat unit postulated in the tobacco mosaic virus structure derived from X-ray diffraction studies. In a similar way, it can be shown that a sedimentation coefficient of 1·9 Svedbergs could not correspond to integral multiples of the 18,000 molecular weight. Comparable low molecular weights have been reported previously for the denatured protein of tobacco mosaic virus[7,8].

Several methods have been used to re-concentrate the diluted tobacco mosaic virus protein. The most successful involved dialysis against a 30 per cent aqueous solution of polyvinylpyrrolidone. Approximately ten-fold re-concentrations and recoveries of 50–70 per cent were obtained for material initially diluted in 0·05μ phosphate buffer at *p*H 7. The re-concentrated protein, adjusted to *p*H 6·5, polymerized into rods when the temperature was raised to 25° C., as described by Lauffer *et al.*[5] for the s_4 component. It was also reconstituted with tobacco mosaic virus nucleic acid into rod-like nucleoprotein particles. Polymerization can be obtained readily. Reconstitution has been completely successful in one experiment; attempts to achieve it under somewhat different conditions of *p*H and ionic strength have thus far failed. Therefore, the dissociated protein must have remained native.

The present work provides the first direct experimental evidence known to us for the existence of a native sub-unit of tobacco mosaic virus protein with a molecular weight agreeing with the value of 18,000 postulated in the interpretation of X-ray diffraction patterns.

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Differences in Chromatographic Patterns of Deoxyribonucleic Acid from Various Tissues

THE constant deoxyribonucleic acid content per set of chromosomes[1,2] and the close similarity of average base composition of deoxyribonucleic acid[3] in various tissues in an animal species can be explained by assuming that the replication of all chromosomal deoxyribonucleic acid initially present in the fertilized ovum follows precisely the Watson–Crick model[4] during the ontogenesis. Recent observations of Bendich *et al.*[5], however, revealed that deoxyribonucleic acid from one animal source is heterogeneous and can be represented as a 'chromatographic profile' as fractionated on an 'Ecteola' cellulose column[6]. Such profiles are different from one tissue to another even in a single mammalian species. The most remarkable difference was found between rat kidney and rat brain. This observation is difficult to reconcile with the Watson–Crick replication model, and suggests a pronounced differentiation of deoxyribonucleic acid during ontogenesis. In repeat-

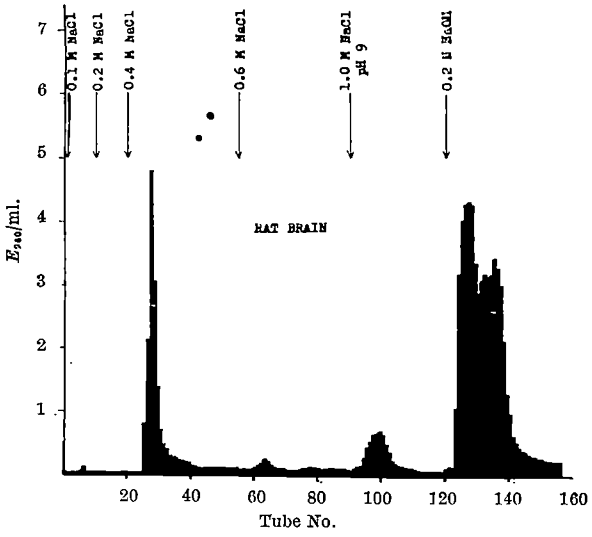

Fig. 1

ing the experiments of Bendich *et al.*, we have obtained a different result, which will be described below.

Twenty adult rats, each weighing about 200 gm., were killed by decapitation. Brain and kidney tissues were quickly removed and immersed in 0·14 *M* sodium chloride–0·01 *M* sodium citrate containing ice. Deoxyribonucleic acid was prepared in parallel from these two tissues by the method of Kay, Simmons and Dounce[7]. The procedure used in the chromatographic fractionation was essentially that described by Osawa and Sakaki[8].

Figs. 1 and 2 show the chromatographic patterns of these preparations. It is clear that no remarkable difference exists between deoxyribonucleic acid from brain and kidney with respect to chromatographic behaviour.

Similar fractionations were carried out on samples of deoxyribonucleic acid prepared from kidney, liver, appendix and testis of adult albino rabbits. In most of these experiments, except for testis, nucleohistone was first prepared according to Mirsky and Pollister[9], followed by the removal of proteins with 'Duponol' by the method of Kay *et al.*[7]. All deoxyribonucleic acids again showed similar patterns in so far as the conditions of preparation and chromatographic fractionation were kept constant. It was, however, found that the sample prepared from nucleohistone and that prepared by the original procedure of Kay *et al.*[7] gave somewhat different pictures. This suggests, as already pointed out by Bendich *et al.*[10], that the chromatographic 'profiles' are largely influenced by the methods of preparation. In any event, we could find no evidence of tissue specificity in this respect, even when the comparison was made on the deoxyribonucleic acids of rat kidney and rat brain, between which the existence of a remarkable difference of 'profiles' had been emphasized[5,11,12].

Discrepancy between our results and those of Bendich *et al.* may be due in part to the different methods of preparation. In our opinion, a reliable procedure for deoxyribonucleic acid preparation applicable to all tissues should be established before any precise chromatographic comparison is attempted.

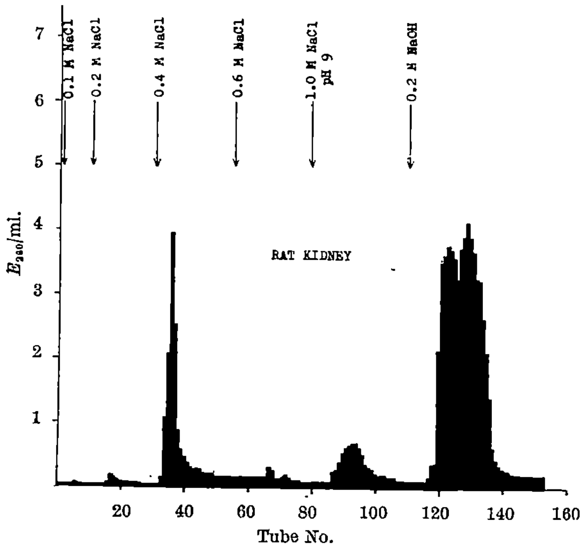

Fig. 2

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Bromination of Nucleic Acids and their Derivatives

RECENT communications on this subject[1–3] have prompted us to report some results of observations which include an extension of work previously described by one of us[4,5].

Suzuki and Ito[1] have reported the effects of bromine on the ultra-violet absorption spectra of some purines, pyrimidines and nucleosides. There was almost complete elimination of the characteristic maxima in the absorption in the region 245–280 mμ, except for adenosine, which was practically unaffected by treatment with the strongest reagent used (1 drop of saturated bromine water to 3 ml. of 7 × 10^{-5} *M* nucleoside).

In the present investigation purines, pyrimidines, nucleosides and nucleotides were treated as follows with bromine water at slightly greater concentrations than those used by previous workers.

A solution (10 ml.) of the substance (0·1 mgm.) in either distilled water or 0·1 *N* hydrochloric acid was treated at room temperature with saturated aqueous

Table 1. Effect of Bromination on the Ultra-violet Absorptio Spectra of Purines, Pyrimidines, Nucleosides and Nucleotides

Compound	Brominated in distilled water	Brominated in 0·1*N* hydrochloric acid
Adenine	Peak at 260 mμ eliminated	Peak at 262·5 mμ unchanged
Adenosine	Peak at 260 mμ unchanged	Peak at 257 mμ unchanged
Adenosine-3′-phosphate, -5′-phosphate, -5′-triphosphate; deoxyadenosine	Peak at 260 mμ slightly reduced	Peak at 257 mμ unchanged
Guanine; guanosine; guanosine-2′(3′)-phosphate	Peaks in the region 245–255 mμ and 275 mμ eliminated	
Cytosine; cytidine; cytidine-2′(3′)-phosphate; deoxycytidine-5′-phosphate	Peak at 267 or 270 mμ eliminated; new peak at 235 mμ	Peak at 275 or 280 mμ eliminated
*Iso*cytosine	Peak at 285 mμ eliminated	Peak at 257 mμ eliminated
Thymine; thymidine; thymidine-5′-phosphate	Peak at about 267 mμ eliminated	
Uracil; uridine; uridine-2′(3′)-phosphate	Peaks at 258 or 262 mμ eliminated	
4-Aminopyrimidine	Peak at 235 mμ almost eliminated	Peak at 245 mμ eliminated

bromine water (0·25 ml.). After 10 min. the bromine was removed by 10 min. vigorous aeration and the ultra-violet absorption spectra of the solutions measured. The results (given qualitatively in Table 1) were in agreement with those reported previously[1] and, in particular, the resistance of adenosine to the action of dilute aqueous bromine was confirmed. Deoxyadenosine and the phosphates of adenosine reacted very slightly with bromine.

The resistance of derivatives of adenine suggested that bromination might be used as a method for the specific degradation of nucleic acids. For this purpose deoxyribonucleic acid (DNA) was treated with bromine as follows:

The deoxyribonucleic acid of calf thymus, isolated by Marko and Butler's method[6] (25 mgm.), was dissolved in 25 ml. of acetate buffer (*p*H 6, ionic strength 0·1) and mixed with 12 ml. chloroform. A solution of bromine in chloroform (1·25 ml.; 10 mgm. bromine/ml.) was added and the solution shaken at 20° C. for 30 min. The mixture was then centrifuged, when a gel layer (not produced by the original deoxyribonucleic acid) was formed at the chloroform–water interface. This was due to the formation of an insoluble gel during the bromination of the deoxyribonucleic acid.

The aqueous and gel layers were combined and treated with ethanol (3 vol.). The precipitate so produced was only partly soluble in water so a suspension of the material was exhaustively dialysed and then freeze-dried to give a yellow solid, designated $BDNA_1$ (22 mgm.).

The deoxyribonucleic acid was also brominated at 2° instead of at 20° C. to give $BDNA_2$ (25 mgm.), and at 20° C., without including chloroform in the reaction mixture and using bromine dissolved in acetate buffer, to give $BDNA_3$ (25 mgm.). These samples were analysed by Dr. D. S. Letham, using formic acid hydrolysis and paper chromatographic separation and estimation of the purines and pyrimidines[7]. The results are shown in Table 2. 5-Methylcytosine was not estimated.

Table 2. Base Composition of Brominated Calf-Thymus Deoxyribonucleic Acid

(Moles of base per 4 atoms of phosphorus)

	Adenine	Thymine	Guanine	Cytosine
DNA	1·10	1·12	0·84	0·86
$BDNA_1$	1·00	0·25	0·12	0·18*
$BDNA_2$	0·95	0·72	0·40	0·49*
$BDNA_3$	0·91	0·60	0·22	0·35*

* Estimated as cytosine, but was probably a mixture.

The identities of the adenine, guanine and thymine in the samples of brominated deoxyribonucleic acid were established by comparison with the R_F values and ultra-violet absorption spectra of the corresponding bases present in the original deoxyribonucleic acid. The cytosine spot on chromatograms of hydrolyses of the brominated deoxyribonucleic acid, although corresponding in R_F value with authentic cytosine, had, in 0·1 *N* hydrochloric acid, an ultra-violet absorption spectrum with a broad flat peak with a poorly defined maximum at 280 mμ. This component was not investigated further, but it was probably a mixture of cytosine with a brominated product ($\varepsilon_{\text{max.}}$ of 5-bromocytidine is at 289 mμ at *p*H 7, ref. 8).

A satisfactory ultra-violet absorption spectrum of the brominated deoxyribonucleic acid was not readily obtainable due to the partly insoluble nature of the material. When $BDNA_1$ was dissolved in 0·1 *N* sodium hydroxide, however, and allowed to stand for 10 min. at 37° C. a drop in the absorption at 260 mμ of 53 per cent as compared with the original deoxyribonucleic acid was obtained. No further reduction in optical absorption occurred on standing at 37° C. for a further 48 hr. The alkali treatment also caused degradation of the molecule as shown by the fact that treatment with 0·1 *N* sodium hydroxide at 37° C. for 15 hr. caused 50 per cent of the material absorbing light at 260 mμ to become dialysable.

Since thymine derivatives were as readily attacked by bromine as were cytosine and guanine derivatives, the relative resistance of the thymine in the deoxyribonucleic acid was remarkable. It appeared possible that the hydrogen bonding of the thymine in deoxyribonucleic acid to the bromine-resistant adenine may have afforded protection to the thymine residues. Another explanation was that some of the thymine may have been regenerated by the acid hydrolysis used to determine the base composition of the brominated deoxyribonucleic acid. The second explanation was supported by the following results.

Derivatives of thymine, cytosine and uracil were treated in aqueous solution with bromine water as previously described. The solutions were next concentrated *in vacuo* and then treated with either 40 per cent formic acid or with 7 *N* hydrochloric acid at 100° C. for 30 min. The solutions were then freed from acid and the ultra-violet absorption spectra determined.

The results (Table 3), some of which are similar to those reported by Cohn[3], suggest that brominated thymine is converted into thymine on acid hydrolysis, whereas brominated cytosine and brominated uracil are not converted into the original bases, but into other ultra-violet absorbing products. The fact that all the thymine and large amounts of a cytosine derivative were not recovered from the hydrolysates of the brominated deoxyribonucleic acid may have been due to the more drastic hydrolysis conditions (98 per cent formic acid at 175° C.) used for the base analysis than for the hydrolysis of the brominated pyrimidines.

Although the adenine in deoxyribonucleic acid was relatively resistant to bromination, it was obvious that considerable destruction of the adenine would occur if bromination of the other bases were carried to completion. It appeared, therefore, that bromine was not so selective as was potassium permanganate

Table 3. ACTION OF ACID ON THE ULTRA-VIOLET ABSORPTION SPECTRA OF BROMINATED PYRIMIDINES

Brominated compound	Treatment at 100° C. for 30 min. with : 40 per cent formic acid	7 *N* hydrochloric acid
Thymine	Spectrum identical with that of the original thymine	
Thymidine-5′-phosphate	As for thymine*	—
Uracil	Peak at 275 mμ, 65 per cent of the height of that of uracil at 260 mμ	Peak at 275 mμ, 90 per cent of the height of that of uracil at 260 mμ
Cytosine	Peak at 277 mμ. Same absorption as that of cytosine at 267 mμ	—

* The solution of thymidine-5′-phosphate after bromination and treatment with formic acid was again treated with bromine water. The peak at 267 mμ was again eliminated.

at 37° C., a reagent, which, as has already been reported[9], oxidized almost completely the guanine, cytosine and thymine in deoxyribonucleic acid, but left 95 per cent of the adenine intact. The latter reagent is, therefore, superior to bromine for the determination of the distribution of adenine in deoxyribonucleic acid.

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Androgens in the Bovine Testis and Spermatic Vein Blood

BULL testis is the organ from which testosterone was first isolated nearly twenty-five years ago[1]. Information is still scarce, however, on the hormone content of this gland at various stages of the animal's development, nor is it known at what age androgenic steroids are first secreted by the gonads in appreciable amounts. Hooker[2] was able to demonstrate the presence of unidentified androgenic material in the testes of prepuberal calves by bioassay. Recent evidence, derived from the chemical analysis of seminal plasma and accessory secretions, indicates that already at the early age of 4–5 months a source of androgens must be present in bull calves, sufficient to induce specific secretory activity in the male accessory glands[3]. The present study was intended to supplement these observations by direct determination of androgenic steroids in the testicular tissue and the spermatic vein blood of the bull.

Material from 25 animals of both dairy and beef breeds, varying in age from 39 days to 17 years, was examined. The 'neutral ketonic fraction' separated from testicular lipid extracts was partially purified by a countercurrent distribution and resolved by paper chromatography in systems developed by Bush[4]. Compounds exhibiting the ultra-violet absorption curve of an α-unsaturated 3-oxosteroid were determined by their absorption at 240 mμ. Additional evidence on the identity of the extracted steroids was obtained by the examination of their absorption spectra in concentrated sulphuric acid and the study of the products formed by acetylation and oxidation or by treatment with Zimmermann's alkaline *m*-dinitrobenzene reagent; finally, purified material was submitted to infra-red spectral analysis. Blood samples were obtained from the spermatic vein of a number of animals and analysed by similar methods. The results were briefly as follows.

Both testosterone (17β-hydroxyandrost-4-en-3-one) and androstenedione (androst-4-en-3 : 17-dione) were identified as constituents of the bull testis at all stages of sexual development, and could be detected at an age as early as 39 days. Per unit weight of tissue, the combined content of the two steroids was not very different in the testes of very young calves (0·4–9 μgm./gm.) and those of fully grown bulls (1–6 μgm./gm.). However, whereas in the mature bull the major testicular androgen was testosterone, in the young calves the predominant steroid was identified as androstenedione. The ratio testosterone/androstenedione was greater than 15 in each of eight adult bulls, but never higher than 0·7 in the eleven calves less than 4 months old.

This pattern was clearly reflected in the steroid composition of the spermatic vein blood. Androstenedione predominated in the blood of 3 months old calves, testosterone in that of adult bulls, while an intermediate ratio of testosterone to androstenedione (approximately 3 : 1) obtained in 4–7 months old calves. Treatment of young male calves with human chorionic gonadotrophin increased both the rate of secretion of androstenedione and its concentration relative to testosterone in the spermatic vein blood. Thus, for example, 0·12 mgm. androstenedione and 0·03 mgm. testosterone were secreted per hr. in the untreated member of a pair of 3 months old monozygous twin calves, while in the other member of this pair, which had received gonadotrophin injections (2,000 I.U./48 hr.) for 7 weeks, the secretion-rate increased to 1·08 mgm. androstenedione and 0·04 mgm. testosterone/hr. By contrast, adult bulls responded to treatment with the trophic hormone with a marked and immediate increase in testosterone secretion. Small amounts of two further steroids were detected by paper chromatography in the spermatic vein blood of gonadotrophin-stimulated calves. Their R_F-values, absorption maxima and behaviour towards acetylating and oxidizing agents and the Zimmermann reagent were those of progesterone and 17α-hydroxyprogesterone (17α-hydroxypregn-4-en-3 : 20-dione).

An additional component was present in a number of extracts of spermatic vein blood collected from bull calves and was shown to be *epi*testosterone (17-α-hydroxyandrost-4-en-3-one). There was reason to believe, however, that this unusual steroid was not secreted as such by the testis, but was formed by the subsequent action of the blood on a substrate of testicular origin. When androstenedione was added to sterile blood (ox or sheep) and the mixture incubated aerobically at 35° C., there occurred a rapid formation of *epi*testosterone, together with smaller amounts of testosterone. This phenomenon was not observed in plasma separated from corpuscles, nor in washed blood corpuscles resuspended in saline.

The present investigation has demonstrated by means of direct chemical determination of steroids that androgenic substances are secreted by the bovine testis into the blood stream already at a very early age. *In vitro* studies by Slaunwhite and Samuels[5] have indicated the following sequence of biosynthetic reactions in rat testicular tissue: Progesterone → 17α-hydroxyprogesterone → androstenedione → testosterone. Our results suggest that the conversion of androstenedione to testosterone may be a rate-limiting reaction in the elaboration of testosterone by the immature bovine testis. A transition to a secretion in which testosterone is predominant would seem to precede the appearance of pubertal changes in this species.

This study is now being extended to other species of farm animals, and in the adult ram, for example, both testosterone and androstenedione were shown to be present in the spermatic vein blood in proportions similar to those found in the bull.

This work has been carried out during the tenure of a scholarship awarded by the Commonwealth Scientific and Industrial Research Organization, while on leave from the Sheep Biology Laboratory, Prospect, N.S.W. I am grateful to Dr. T. Mann for his counsel and continued stimulating interest, to Dr. R. V. Short for advice, and to Mr. L. E. A. Rowson for his generous help in collecting animal material.

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Acid Mucopolysaccharides of Normal Urine

The occurrence of at least one acid mucopolysaccharide in normal urine has repeatedly been reported[1-3]. It was found by various authors[1-3] to behave chromatographically and electrophoretically like chondroitin sulphate *A*. Separation and staining, however, were unsatisfactory.

We recently described[4] a convenient and highly specific staining method for acid mucopolysaccharide in which use was made of a 1 per cent solution of alcian blue (Gurr or Harleco) in a 9 : 1 mixture of acetic acid and water (5 min.), followed by alternate washings with acetic acid and tap water. The intensely blue acid mucopolysaccharide spots stand out on a pure white background, and as little as 0·5 μgm. of heparin or 2·0 μgm. of chondroitin sulphate *A* can be detected. Scanning allows quantitative estimations, since the uptake of dye appears to be proportional to the acid mucopolysaccharide concentration over a wide range. A correction factor is nevertheless required to allow for different specific dye uptakes by different acid mucopolysaccharides.

By using an ultrafiltration and dialysis method, to be described elsewhere, it was possible to concentrate normal urines up to 3,000 times without any denaturation of their colloids. Electrophoresis on Whatman No. 1 filter paper in a veronal–acetate buffer of *p*H 8·6 and ionic strength 0·1, using 3 V./cm. for 12 hr., resulted in very sharp separation of three different acid mucopolysaccharides, which migrated ahead of the albumin peak. The fastest and most abundant peak migrated about twice as fast as albumin, and at exactly the same speed as commercial chondroitin sulphate *A*. This is presumably the substance described by other authors[1-3]. The second peak, which was usually though not always smaller than the first, had a mobility of about 1·5 times greater than albumin. The third and smallest peak was about 1·1 times faster than albumin. None of these substances could be stained by protein dyes.

Fig. 1. Urinary acid mucopolysaccharides separated by electrophoresis at *p*H 8·6 and stained with alcian blue. The albumin (unstained) is indicated by arrows

All three appeared to have some anticoagulant activity of the heparin type, which casts considerable doubt on their identification as chondroitin sulphates *A* or *C*, which are known to be devoid of anticoagulant properties. On the other hand, commercial alpha-heparin samples ('Liquaemin', Roche) was found to migrate distinctly faster than the fastest urinary acid mucopolysaccharide peak.

The identification of these three substances must await further investigation, which is now in progress in our laboratory.

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Persistence of Cholesterol-4-^{14}C in the Central Nervous System

Recent work from this laboratory[1,2] has shown that once cholesterol-4-^{14}C is incorporated into the central nervous system of developing rabbits and chickens it remains with little change for more than a year. It seems likely that this radioactive cholesterol is incorporated into the myelin sheath, but there remains the possibility that once in the central nervous system the cholesterol undergoes internal turnover, being broken down and resynthesized *in situ*. This communication presents evidence to show that the radioactive carbon atom, even after 18 months, remains in its original position in the cholesterol molecule. In these experiments cholesterol extracted from the central nervous system with chloroform–methanol (2 : 1) was isolated by fractionation on an alumina column. The cholesterol was converted to cholestenone by an Oppenauer oxidation[3]. Next the radioactive cholestenone was ozonized

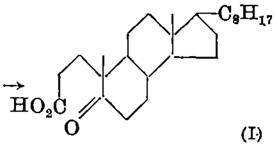
Table 1. Localization of Radioactivity in the Cholesterol Ring

Time after injection (days)	Dose given (μc.)	Specific activity (c.p.m./mgm. of cholesterol or its equivalent)			
		Crude extract	Cholesterol	Cholestenone	Keto-acid (I)
375 (rabbit)	5	45	47	35	1·8
502 (chicken)	3	22·9	23·4	14	0·96

A crude lipid extract in alcohol–ether (3 : 2) or chloroform–methanol (2 : 1) was obtained from the central nervous system of animals injected with cholesterol-4-^{14}C soon after birth. Pure cholesterol was obtained by recrystallization of cholesterol separated from the crude extract by column chromatography. Cholestenone and the keto-acid were prepared as described below.

and then oxidized with hydrogen peroxide by the method of Turner[4]. The keto-acid (I) obtained as a result of this elimination of a carbon atom at position 4 was purified and recrystallized. The melting point was in agreement with that reported in the literature[4,5]. Comparison of the radioactivity of the cholesterol with the radioactivity of the keto-acid (Table 1) shows that almost all the activity disappears on elimination of the 4-C atom. Furthermore, it was found that all the radioactivity in the original crude extract of the central nervous system was due to its content of radioactive cholesterol (Table 1). This latter result also suggests that the cholesterol molecule remains intact in the central nervous system for more than a year, for if the cholesterol-4-^{14}C had been degraded it would be anticipated that other radioactive lipids would be synthesized from the resultant fragments. These two groups of experiments, therefore, support the view that the cholesterol that persists in the central nervous system remains metabolically inert for more than a year.

Cholesterol→ Δ^4-cholesten-3-one →



(I)

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A Simplified Physico-chemical Method for Determination of Human Urinary Œstrogens

The methods for estimating urinary œstrogens are open to criticism and are not easily applied as a routine in the laboratory because of their complexity. Our chief aim in the present investigation is to develop a reliable, practical and simplified method for studying the excretion of urinary œstrogens by patients with cancer of the breast.

100 ml. urine of 24-hr. sample was adjusted to *p*H 5 with concentrated sulphuric acid. 10 per cent by volume of acetate buffer was added, followed by 300 Fishman units of β-glucuronidase/ml. urine. This was incubated at 37° C. for five days[1]. After completion of hydrolysis, the urine was extracted four times with 100 ml. peroxide-free ethyl ether. The ether extract was washed with (*a*) saturated sodium carbonate solution, *p*H 10·5, (*b*) 2 *N* sodium hydroxide solution which was neutralized to *p*H 10 with 8 per cent sodium bicarbonate solution and shaken again with the ether extracts, (*c*) 8 per cent solution of sodium bicarbonate, (*d*) water[2]. The ether extract was evaporated to dryness and the residue dissolved in about 80 ml. toluene; this was extracted four times with 0·25 volume *N* sodium hydroxide and washed twice with 0·05 volume water. Neutral steroids remain in toluene layer. Alkaline extracts and washings were acidified to *p*H 9 with sulphuric acid (6 *N*) and extracted four times with 0·25 volume ether. This was evaporated and the residue was transferred to small storage bottles with methyl alcohol and evaporated to dryness at 60° C. Counter-current distribution in 50 per cent methanol, 50 per cent water (upper layer)/carbon tetrachloride (lower layer)[3] was then carried out for 24 transfers. Œstrogen extract was dissolved in 0·2 ml. ethanol and heated in a water-bath with 1 ml. 90 per cent sulphuric acid at 80° C. for 10 min. This was diluted with 4 ml. 65 per cent sulphuric acid and cooled in crushed ice for 30 min. Fluorescence was measured in a Farrand photofluorometer model *A* using Corning glass No. 3389 and No. 5113 as the lamp filter (436 mμ) with Nos. 3387 and 4308 and a 483 mμ interference filter as the photocell filter[4–6].

The specificity, precision and accuracy of the newly developed technique are shown in Table 1. These results were obtained by running a series of recovery experiments for the three major naturally occurring œstrogens.

Table 1. Recovery of Œstrone, Œstradiol-17β and Œstriol added to 100 ml. of Normal Male Urine before Hydrolysis

Œstrogen used	Amount added (μgm.)	Percentage recovery	Partition coefficient*
Œstrone	100 50	85 82	3·4
Œstradiol-17β	100 50	91 87	2·1
Œstriol	100 50	93 94	15·3

* Between 50 per cent methanol and carbon tetrachloride.

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Effect of Drugs upon Components of Bacterial Cytoplasm

ULTRACENTRIFUGAL analysis has shown that one of the main ribonucleoprotein components of bacterial cytoplasm is sensitive to alterations in the concentrations of certain salts present in the growth medium, or in the medium in which cells are suspended before they are disrupted[1-3]. This component sediments at about 40S. (uncorrected) and its breakdown within whole cells is favoured by lowering the concentration of magnesium ions or raising that of inorganic phosphate; ribonucleoprotein particles sedimenting at about 29 and 20S. are relatively insensitive to these extracellular changes in concentration.

It does not appear that the 40S. component plays any part in the metabolism of the cell which other ribonucleoprotein units of smaller molecular weight cannot share. For example, when bacteria were depleted of this component their ability to synthesize β-galactosidase was not impaired[4]. A connexion between bacterial cell-division and stability of the 40S. component is suggested by the requirement of both processes for magnesium ions. Accordingly, we examined cultures grown in the presence of 5 I.U. penicillin/ml., which stopped cell-division but allowed synthesis of cellular material to proceed, so that the whole culture eventually consisted of filamentous cells several times their normal length. However, no change was observed when schlieren diagrams were compared; the amount of 40S. component present in extracts from filamentous cells was the same as that from normal cells.

These results stand in contrast to those obtained for 'Chloromycetin' (chloramphenicol). *Escherichia coli* was grown in the medium containing peptone, glucose and inorganic phosphate as previously described[2] except that the concentration of magnesium sulphate was raised to 6·5 m*M* to avoid breakdown of the 40S. component at high cell populations[4]. During an incubation period of 150 min. five samples were removed at intervals from a control culture and, after centrifuging, the cells were disintegrated in bacterial presses[5], and five soluble cell-free extracts were obtained. The experiment was repeated using *E. coli* cells from the same overnight grown culture for inoculation but with addition of 5 μgm. of 'Chloromycetin'/ml. of growth medium; this caused a lag in both growth and cell-division, and no filamentous bacteria were observed. Ultracentrifugal analysis showed that this treatment with 'Chloromycetin' caused marked alterations in schlieren diagrams of extracts. Incubation with the drug for 30 min. resulted in a considerable increase in area of a peak sedimenting at 18S. and the appearance of a new peak at 14S.; both increased further during the lag period. In Fig. 1, schlieren diagrams for extracts from cells incubated for 30 and 150 min. with 'Chloromycetin' are contrasted with one of those obtained in the absence of the drug. Previously[2], prominent components have been designated 40, 29 and 20S. for ease of reference, although these values are subject to variations, particularly in the crude extracts studied; in the present series the measured values are respectively about 35, 22 and 18S. The additional material responsible for enlargement of the peaks at 18 and 14S. is probably the 'unstable ribonucleic acid' sedimenting as nucleoprotein, which other workers have shown to be synthesized by bacteria in the presence of 'Chloromycetin'[6-8]. A small peak sedimenting a little faster than 22S. is also seen in diagram (*b*); this was not present in diagrams for the control or in those taken later in the lag phase for cells treated with 'Chloromycetin'.

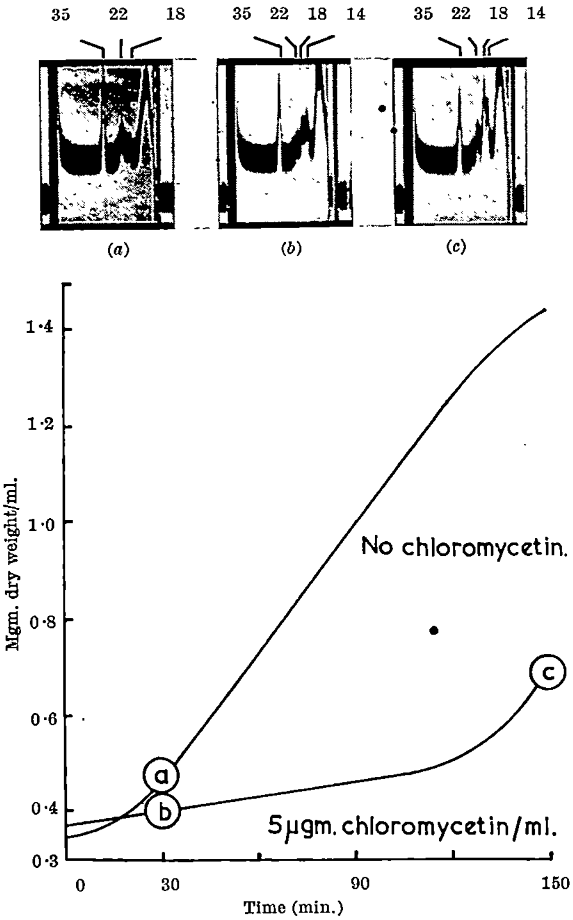

Fig. 1. Schlieren diagrams of extracts from cells (*a*) untreated, and (*b*) and (*c*) treated, with 'Chloromycetin'. Cell-free extracts were prepared in 0·06 *M* phosphate buffer at times indicated on the growth curves and were each diluted to 10 mgm. protein/ml. Photographed of the same schlieren angle (41°) at 16 min. after reaching speed of 187,000*g*. The numbers above the photographs give the uncorrected sedimentation coefficients of boundaries in Svedberg units

A second effect of 'Chloromycetin' is that produced on the '29S. component', which in Fig. 1 has a measured coefficient of 22S. As the 18 and 14S. peaks enlarged in the early part of the lag period due to the drug, so the 22S. peak diminished; and when cell-division began at 120–150 min., the 22S. peak increased rapidly in area, as can be seen by comparing diagrams (*b*) and (*c*). The area of the 35S. peak changed little during these experiments. An increase in the '29S. component' at the onset of logarithmic growth is normally observed[2]; further, this component remains when '40S.' breaks down due to changes in ion concentrations which do not impair cellular metabolism. If ribonucleoprotein particles of a critical size have a specific role in, say, synthesis of bacterial protein, then the '29S. component' appears from the present work more likely to be involved than larger units. Attempts to assign particular functions in the living cell to components of preparations made from them must always take account of the possibility that particles may have arisen simply by mechanical disintegration of larger structures. Smaller units do not always arise from such processes, however ; thus, the ribonucleoprotein components of bacterial cytoplasm tend to aggregate or associate in the presence of magnesium ions ; and unless the concentrations of these and other ions in extracts approximate to those in the living cell, the larger particles may have no greater metabolic significance than the smaller ones.

Pardee, Paigen and Prestidge[8] also found that the '29S. component' disappeared from extracts of cells which had been incubated with 'Chloromycetin' but they found no additions to the schlieren diagrams at 18 and 14S. such as we have described. However, until we have completed work on the factors affecting stability of this additional material, it must not be concluded that our results are opposed to those of Pardee *et al.* Thus we have studied cultures containing the rather high concentration of 6·5 mM magnesium sulphate which favours ribonucleoprotein association ; and it has been observed that degradation of ribonucleic acid formed during 'Chloromycetin' treatment is rapid when cells are suspended in phosphate buffer[6], conditions which also favour breakdown of the ribonucleoprotein particle sedimenting at 40S.

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Effect of Salicylate on Muscle Phosphorylase

During the course of an investigation of the effects of salicylate on glucose metabolism it was observed that incubation of the isolated rat diaphragm in a Krebs–Ringer bicarbonate medium containing salicylate caused a loss of glycogen from the muscle. Such an observation had been made previously by Smith and Jeffrey[1], who employed a phosphate medium with higher levels of salicylate. Under the conditions of our experiments, however, the loss of glycogen from the diaphragm occurred mainly within the first 30 min. of incubation and thereafter occurred at a much slower rate despite the fact that muscle glycogen was still present in abundant amounts (a paper describing this and other effects of salicylate on glucose metabolism is in preparation). In an attempt to explain the alteration in rate of glycogenolysis occurring after 30 min., assays were carried out of active (*a* form) and total (*a* + *b* form) phosphorylase present in the muscle.

Fed male Sprague–Dawley rats (150–175 gm.) were killed by stunning and decapitation. 3–4 isolated hemidiaphragms were placed in a 25-ml. flask with 5 ml. of Krebs–Ringer bicarbonate medium *p*H 7·4 containing 100 mgm. glucose and 30 mgm. salicylate/100 ml. (this is a concentration of salicylate which when present in human blood is in the nearly toxic range). As a control, the paired hemidiaphragms were placed in medium without salicylate. After being gassed with 95 per cent oxygen, 5 per cent carbon dioxide for 30 sec., the flasks were stoppered and incubated for varying periods of time in a Dubnoff shaker at 37° C. At the end of the incubation a 10 per cent homogenate of the diaphragms was made in the cold with a Potter–Elvejhem homogenizer, using 0·01 M disodium versenate in 0·01 M phosphate buffer *p*H 7·4 as the homogenizing fluid. The homogenate was centrifuged to precipitate cell debris, and the supernatant fluid was diluted 1 : 8 with cysteine-glycerophosphate buffer *p*H 6·0.

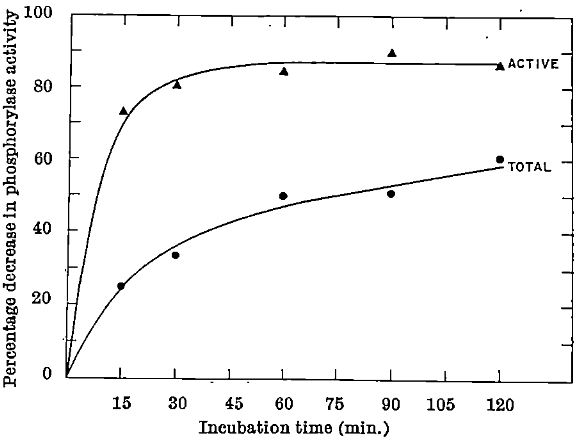

Fig. 1. Effect of incubation with salicylate on muscle phosphorylase in rat diaphragm

The phosphorylase activity of the supernatant fluid was assayed by Cori, Illingworth and Keller's method[2] and expressed as μM inorganic phosphorus[3]/mgm. of protein[4] in 20 min. Concomitant determination of glycogen[5] revealed that glycogen was synthesized in stoichiometric amounts to inorganic phosphorus liberated. When phosphorylase activity was measured by synthesis of glycogen, the findings with salicylate paralleled those obtained by measuring liberation of inorganic phosphorus. Phosphoglucomutase activity was minimal in both control and salicylate-treated preparations.

The results are shown in Fig. 1, each point representing an average of two experiments. At the end of a 15-min. incubation of the diaphragm with salicylate a 70 per cent decrease in active phosphorylase (*a* form) had occurred, eventually reaching about an 87 per cent decrease in activity. Total phosphorylase (*a* + *b* forms) showed a decrease in activity but at a much slower rate. In representative experiments shown on Table 1 the quantity of active phosphorylase in the controls ranged from 34 to 50 per cent of the total amount of enzyme present. This was reduced to 10 per cent by incubation with salicylate for 1 hr.

Since salicylate has been known to uncouple oxidative phosphorylation[6], experiments were performed with dinitrophenol, another uncoupling agent. Table 1 demonstrates that dinitrophenol produces a similar effect on muscle phosphorylase. On the other hand, parahydroxybenzoate, an isomer of salicylate, caused no decrease in the enzyme activity. Studies carried out on crystalline rabbit muscle phosphorylase

Table 1. THE EFFECT OF SALICYLATE, DINITROPHENOL AND *p*-HYDROXYBENZOATE ON PHOSPHORYLASE IN RAT DIAPHRAGM INCUBATED 60 MIN.*

Experiment	Active enzyme	Total enzyme
	(μM inorganic phosphorus/mgm. protein)	
1 Control	8·1	18·2
Salicylate† 30 mgm. per cent	1·3	11·6
2 Control	4·8	14·0
Dinitrophenol 2 mgm. per cent	0·5	5·3
3 Control	9·3	18·5
p-Hydroxybenzoate† 30 mgm. per cent	11·0	22·4

* Average values for two experiments.

† Sodium salt.

showed that salicylate in the concentration used in the diaphragm experiments produced no decrease in enzymatic activity of the crystalline material (obtained from Sigma Chemical Co., St. Louis, Mo., 2,000 U./mgm. all in active form).

In one group of experiments epinephrine hydrochloric acid (10 γ/ml.) was added to the media after the diaphragm had been incubated with salicylate for 30 min. During subsequent incubation for an additional 60 min., epinephrine increased the active phosphorylase by more than 100 per cent of the low value found in diaphragms incubated with salicylate a total of 90 min. Epinephrine had little or no effect on the level of total phosphorylase.

Since salicylate does not affect the activity of the crystalline enzyme, the decrease in phosphorylase activity in the diaphragm resulting from salicylate treatment is probably a secondary effect on one or more factors necessary for maintenance of the *a* and *b* forms of phosphorylase in the muscle. The initial and most profound effect is a decrease in active phosphorylase which could result either from a stimulation of the *PR* enzyme[7] converting the *a* to the *b* form, or from an inhibition of the activating enzyme[8] which converts *b* to *a* and which is dependent on adenosine triphosphate. The slower decrease in total phosphorylase suggests that the *b* form normally activated by adenosine-5′-phosphate is converted to a form no longer activated by the nucleotide. The effects of salicylate on phosphorylase would adequately explain the observed effects of this compound on the rates of glycogenolysis in the diaphragm.

We wish to express our thanks to Dr. Marshall Nirenberg for his helpful suggestions during the course of this work.

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CHEMISTRY

5-Co-ordination of Divalent Copper

CONSIDERABLE attention has recently been given to the co-ordination of additional ligands along the axis normal to the molecular plane of planar 4-co-ordinated complexes. Ballhausen and Liehr, for example, explain the blue and yellow isomers of Lifschitz's nickel stilbene-diamine salts in terms of co-ordination of the associated anions in this way[1]; Harris, Nyholm and Stevenson have shown by X-ray analysis the analogous attachment of iodide ions in *bis*-(*o*-phenylene-*bis*-dimethylarsine)palladous iodide[2] and Sacconi, Lombardo and Paoletti have determined stability constants for the adducts of heterocyclic bases with the planar inner-complex nickel diacetyl-*bis*-(benzoylhydrazone) in benzene solution[3].

The resistance of planar complexes of divalent nickel, palladium and platinum to further co-ordination derives from the effect of the ligand field in so raising the energy of the $d_{x^2-y^2}$ orbital, which points directly at the ligands, that it remains unoccupied; the consequent pairing of electrons in the d_{z^2} orbital produces regions of high electron density normal to the molecular plane, so resisting the approach of further ligands[4]. A similar situation arises in planar cupric complexes (the $d_{x^2-y^2}$ orbital being then singly occupied), and the elongated octahedral co-ordination of this ion in crystalline salts has been known for many years[5]; but apart from this, comparatively little attention has been given to co-ordination of further groups normal to the molecular plane of cupric complexes, though the solubilities of cupric α-amino-acid chelates suggest that solution may occur by co-ordination of water in this way[6].

It thus seems of interest to report the formation in non-polar solvents of 5-co-ordinated complexes by attachment of heterocyclic bases to the planar molecules of cupric acetylacetonate and cupric ethylacetoacetate.

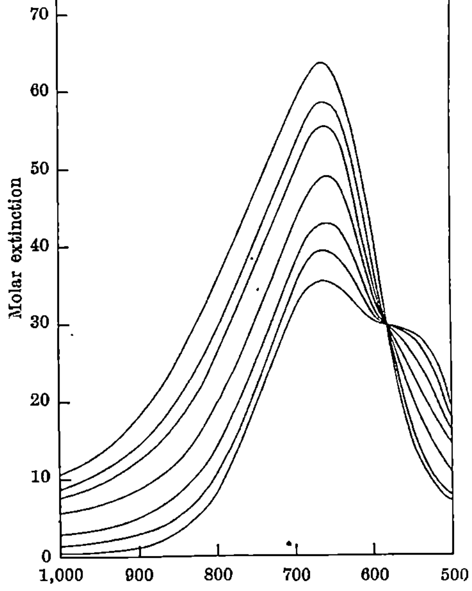

Fig. 1. Absorption spectrum of cupric acetylacetonate in chloroform with increasing concentrations of pyridine

The absorption of cupric acetylacetonate in chloroform solution is considerably modified on addition of pyridine, most noticeably by a progressive increase in extinction of the peak at 660 mμ with increasing concentration of the base. The successive absorption curves have a sharply defined isosbestic point (Fig. 1), indicating a two-phase equilibrium. The equilibrium constant, calculated from the molecular extinctions, is of the form :

$$k = \frac{[\mathrm{Cu(acac)_2.pyridine}]}{[\mathrm{Cu(acac)_2}] \times [\mathrm{pyridine}]}$$

showing that only one molecule of pyridine is co-ordinated. Though formation of the 5-co-ordinated complex is incomplete, even with a two hundred-fold excess of pyridine, the equilibrium constants are so consistent over the whole range that any alternative form of the equilibrium constant, such as that required for 6-co-ordination, can be excluded. Thus, at 20° C. with 5×10^{-3} *M* cupric acetylacetonate the results in Table 1 were obtained. Similar results were obtained with piperidine ($k = 3 \cdot 3$; extrapolated extinction of complex = 86·5). It is significant that the extrapolated absorption curves of the pyridine and piperidine complexes are, within the limits of error, identical with those observed by Belford, Calvin and Belford[7] using pure pyridine or piperidine as solvents, so that any possibility of the completion of 6-co-ordination by the solvent may be discounted. This possibility would not arise in paraffin solvents, but the solubility of cupric acetylacetonate in these is too low to allow their use ; cupric ethylacetoacetate, however, is much more soluble in paraffins, and parallel results have been obtained for its reaction in *cyclo*hexane solution at a concentration of 10^{-3} *M* with piperidine ($k = 640$; extrapolated extinction = 83), pyridine ($k = 54$; extrapolated extinction = 76), γ-picoline ($k = 36$; extrapolated extinction = 77) and α-picoline ($k = 4 \cdot 9$; extrapolated extinction = 76).

Table 1

Pyridine (*M*/l.)	0	0·045	0·105	0·195	0·400	0·600	1·00	∞
ε (660 mμ)	35·6	39·4	43·0	47·8	55·5	58·5	63·8	75·6*
Cu 5-co-ordinated (per cent)	0	9·5	18·5	30·5	49·5	57·0	70·5	100
k (mean = 2·3)	—	2·33	2·15	2·25	2·45	2·22	2·39	—

* Extrapolated.

The general trend of the equilibrium constants for combination with cupric ethylacetoacetate is similar to that observed by Sacconi, Lombardo and Paoletti[3] for co-ordination to nickel, including the low value for α-picoline, no doubt due to steric interference by the methyl group. The much lower stability of the acetylacetonate adducts suggests that the copper atom in these carries a much smaller net charge, as would be expected from general considerations of structure and from the polarographic results of Calvin and Bailes[8], though a small part of the effect may be due to the change of solvent.

The use of *cyclo*hexane as solvent eliminates any possibility of co-ordination by the solvent and these stability constants thus share with those of Sacconi, Lombardo and Paoletti the unusual property of referring to a process of co-ordination uncomplicated by the displacement of co-ordinated solvent molecules, implicit in all equilibria observed in aqueous solution.

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Detection and Estimation of Benzenoid Compounds by Chromatography

METHODS have frequently been described for the detection and estimation of heterocyclic compounds on chromatograms by ultra-violet photography[1-4]. These methods use a mercury discharge lamp suitably filtered. This type of lamp, however, yields predominantly the 253·7 mμ mercury line and is only suitable for compounds having a considerable absorption at this wave-length. With the benzenoid ring class of compounds, the absorption maxima are generally between 265 mμ and 285 mμ, frequently with the trough near the 253·7 mμ line. Consequently, in order to detect these compounds by a similar technique, a different source of light is necessary.

Table 1

Compound	Absorption	
	Maximum (mμ)	Minimum (mμ)
cis-trans β-Chloromuconic acid	264	—
cis-cis Muconic acid	259	—
2-Hydroxy-4-chlorophenoxyacetic acid	283	255
4-Chloroguiacol	283	255
p-Chlorophenoxyacetic acid	280	247
4-Chlorocatechol	284	250

A hydrogen discharge lamp, similar to that used in the 'Unicam' quartz spectrophotometer (*S.P.* 500), was used as the source of ultra-violet light, utilizing the stabilized power unit of the *S.P.* 500. It was necessary to reduce the continuous spectrum of the hydrogen lamp to a band of 260–300 mμ with a peak at 285 mμ. An aqueous nickel sulphate solution (27·5 gm./200 ml.) has a high transmission of light between 220 mμ and 360 mμ and also above 400 mμ. An aqueous solution of quinine sulphate (125 mgm./250 ml. + 1 drop of sulphuric acid) transmits a band between 260 mμ and 290 mμ and also above 360 mμ. A mixture of three parts nickel sulphate solution to one part of quinine sulphate combined with a 'Chance' *OX* 7 filter, to cut off the visible light, provided a suitable stable filter system. The transmission curves of the component filters are shown in Fig. 1. The filter compartment comprised of the *OX* 7 filter as one face and a quartz plate as the other (3 in. × 3 in., optical faces) with a rubber cushioned 'Perspex' 'U' (4 in. × 4 in. × ½ in., diameter of central hole being 2 in.) separating the two. Two brass plates (4 in. × 4 in. × ¼ in.) with 2-in. diameter holes cut centrally, also rubber-cushioned, were placed at each end of the compartment and the whole bolted together at the corners with brass bolts to a suitable lamp

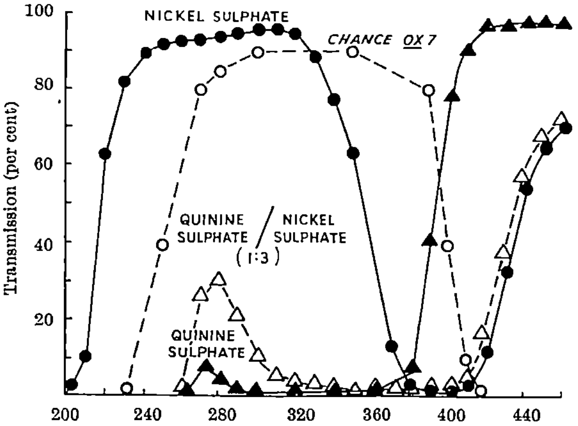

Fig. 1. Transmission spectra of filters

housing. A heat–light baffle was made at the top of the lamp housing. The chromatogram from which the solvent system had been completely removed was stretched tightly over Ilford bromide document paper No. 60 and exposed to the light source. The exposure was approximately 30 sec. at 2 ft. Table 1 shows the absorption maxima and minima of some metabolic intermediates which were resolved in this manner[5-7]. It was possible to trace the spots on to the chromatogram, and after elution estimate them quantitatively in the ultra-violet spectrophotometer. 0·10 μmole of *cis-trans* β-chloromuconic acid, 1 μmole of 2-hydroxy-4-chlorophenoxyacetic acid and 1 μmole 4-chlorocatechol could be estimated in this way.

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Melting Point and Sublimation of Molybdenum Disulphide

Molybdenum disulphide has until recently been reported as having a melting point[1] of 1,185° C. In 1956, however, Zelikman and Belyaevskaya[2] reported that samples of molybdenum sulphide did not melt at temperatures up to 1,350°, and only those which had been heated to temperatures in excess of 1,650° C. showed any (microscopic) signs of melting. The purpose of the present communication is to report experiments made in connexion with the preparation of clean molybdenum disulphide surfaces, which are relevant to the question of the melting point of the material.

By heating pure powdered molybdenum disulphide, suspended from a quartz spiral, *in vacuo*, plots of weight vs. temperature were obtained. The sample was purchased from the Alpha Molykote Corp. of Stamford, Conn., and contained 58·9 per cent molybdenum (calc. for molybdenum disulphide, 60·0 per cent). The sensitivity of the system was about 0·5 per cent of the sample weight and the ultimate vacuum in the system better than 10^{-6} mm. mercury. The heated zone of the apparatus was made from fused quartz. Apart from losses in weight at lower temperatures due to the evolution of material adsorbed from the atmosphere, the weight losses of interest are one of about 2 per cent in the temperature 850–950° C., which presumably corresponds with the volatilization of surface molybdic oxide, and a much larger one at temperatures in excess of 1,050° C., when a brown film begins to cover the inside of the apparatus. This film, when examined by the electron-diffraction technique, proved to be hexagonal molybdenum disulphide. The weight loss at this highest temperature was proportional to the time the specimen was held at that temperature. The residual solid was observed to be a loose sinter of no great mechanical strength, even after the sample had been held at 1,250° C. for 4 hr. At this temperature, the quartz wall was attacked by the deposited molybdenum disulphide, with the formation of a zone of powdered silica. The net result was the ultimate devitrification of the apparatus.

Table 1

Sample No.	Temperature, °C (± 20°) at which sample was taken	Gas pressure (μ)	Composition in sample bulb
1	1,000	2	CO or N_2 + a little H_2
2	1,200	11	CO or N_2
3	1,450	0·03	CO or N_2
(Sample was allowed to cool and experiment recommenced after the system had been pumped down (once more, hard))			
4	980	2	95 per cent CO 5 per cent H_2
5	1,400	0·8	85 per cent CO 15 per cent H_2
6	1,510	1	88 per cent CO 12 per cent H_2
7	1,720	0·5	85 per cent CO 15 per cent H_2
8	1,800	0·3	75 per cent CO 25 per cent H_2

A pair of specimens of pure natural massive molybdenite (locality Kingsgate, New South Wales, molybdenum obs. 58·4 per cent, no other metals present to the extent of more than a trace except lead, 0·01 per cent) were mounted by molybdenum bolts to molybdenum leads in such a way that the resistance, and hence the continuity, of the specimens could be checked. A molybdenum crucible was arranged around the specimens, the assembly placed in a quartz envelope, and attached to a high-vacuum pumping system via a gas sample manifold. The specimens were heated inductively, and the evolved gases were sampled and afterwards analysed on a mass spectrometer (Table 1). Surprisingly, the gases contained no sulphur-bearing materials at all. Temperatures were measured using a calibrated disappearing-filament pyrometer, with suitable corrections for the emissivity of molybdenum metal as viewed through quartz. Quartz strip shields were used to prevent the formation of a continuous condensed film of the sample around the wall, which would have caused coupling of the radio-frequency field with the conducting deposit, and which also would have prevented accurate observation of the temperature of the crucible.

The specimens did not melt even when held at a temperature of 1,800±20° C. for 10 min. Consequently, the melting range of 1,650–1,700° reported by Zelikman and Belyaevskaya[2] cannot be real: their result may be due to reaction of the sample with its surroundings since they used graphite vessels. Such an artefact is certainly the cause of the very low early value of 450° C. due to Joly[3] for the onset of sublimation of molybdenite, which in this work occurred around 1,050° C. If molybdenum disulphide obeys the Tammann rule, that is, if it begins to sinter noticeably at a temperature about one-half of its absolute melting point[4], then it would be expected to have a melting point around 2,375° C.

I wish to thank J. Kelly for preparing the vacuum systems and F. J. Norton for the mass spectrometric gas analyses.

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Alicyclicity and Smoke Emission of Coal

MUCH work has been done in the past on the smokiness or the smoke nuisance of coal during combustion, but mainly on its abatement. The fundamental causes of smoke emission have been little studied, though its obvious link with volatile matter and/or tar[1] has been known. Recent dehydrogenation studies[2,3] made by us leading to the determination of alicyclic carbon in coal have resulted in certain findings on the pyrolysis and combustion behaviour of dehydrogenated coals which obviously suggest that alicyclic bodies in coal are the main smoke-forming constituents.

It has been shown elsewhere[3] that dehydrogenated coals (for example, by Vesterberg's technique—dehydrogenation carried out with sulphur below the decomposition point of coal) do not yield any tar and that the char yield increases proportionately to the alicyclic carbon content of coal at the expense of tar-forming bodies. It has been shown[4] that alicyclic bodies in coal are primarily responsible for the formation of tar.

These findings naturally prompted us to study the combustion behaviour of the dehydrogenated coals. As the devolatilization of alicyclic bodies, that is, the tar-forming bodies, is completely inhibited on dehydrogenation, it was anticipated that pyrolysis of such bodies would also be avoided during combustion, resulting possibly in the smokeless burning of such coals. This was found to be so in the case of all dehydrogenated coals prepared from different ranks.

Table 1. ALICYCLICITY AND SMOKINESS OF COAL

Coal	On unit coal (per cent)			
	Carbon	Hydrogen	Alicyclic carbon*	'Smokiness'†
Assam	80·3	5·9	16·1	2·44
Jambad Bhowlah	80·6	5·4	13·7	2·25
Poniati	83·5	5·5	15·5	2·25
Laikdih‡	87·3	5·3	10·1	1·50
Pootki‡	88·0	5·3	11·2	1·40
Jharia, IX	90·7	4·7	5·5	0·87
Jharia, IX	90·4	4·6	3·6	0·75
Anthracite (South Wales)	93·2	3·5	nil	nil

* Data taken from earlier papers (refs. 2, 3 and 4).

† By 'smokiness' is meant here the soot and free carbon in the flue gas which was trapped and filtered off quantitatively in glass-wool and weighed. The experiments were carried out in a small muffle furnace under identical conditions of air-supply, that is, the ratio of air to the amount of volatiles was kept the same in all cases by adjusting the weight of coal.

‡ Vitrains.

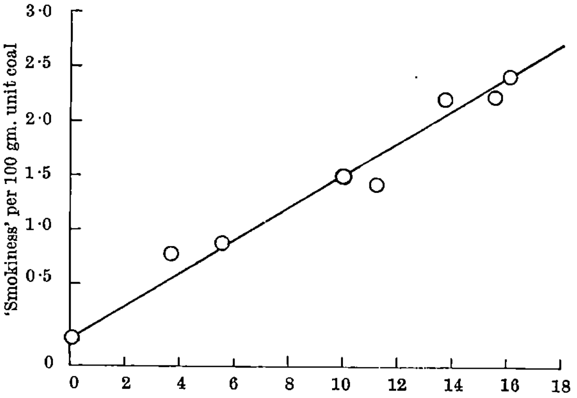

Fig. 1. Relation between alicyclicity and smoke emission of coal

Halogenation also has been found[5] to bring about the same type of dehydrogenation and stabilization of alicyclic carbon during subsequent pyrolysis. Such dehydrogenated coals are also smokeless during combustion. Prior treatment of coal with acids like sulphuric and phosphoric and certain other dehydrating agents like phosphorus pentoxide and potassium hydrogen sulphate also renders a coal smokeless without having to carbonize it. It has been found that during such treatment no tangible loss of carbon or hydrogen takes place, but apparently a reorganization (possibly condensation) of the alicyclic part in relation to the basic aromatic nucleus occurs whereby devolatilization of alicyclic bodies is completely inhibited[6].

Controlled oxidation[7] of any coal will also bring about a similar change.

It would appear, therefore, that smoke emission is primarily due to the alicyclic structures in coal and any process which can help stabilize such structure would make a coal smokeless.

Relative smokiness of different ranks of coal has been measured (Table 1) and is found to bear a linear relationship with alicyclic carbon content of the coals (Fig. 1). Anthracites and semi-anthracites contain very little or no alicyclic carbon, and hence they are smokeless. Semi-coke or char are smokeless fuel as these carbonized products do not contain any alicyclic structure. Thus it is possible to make a smokeless fuel from any coal without having to carbonize it. The inhibition of tar formation on oxidation of coals has been known for a long time; but the fundamental causes have become evident from our studies on dehydrogenation of coals.

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Density of Water sorbed on Montmorillonite

A RECENT communication by R. C. Mackenzie[1] on the above subject directs attention to some density measurements made on Wyoming bentonite pastes[2,3]. A confirmatory set of measurements has also since appeared[4]. Although the results were not obtained under exactly comparable conditions or on exactly comparable material, they exhibit adequate internal consistency. The divergences seem to arise in the authors' discussions.

Fig. 1 presents a plot of density versus weight per cent of oven-dry bentonite in the pastes reduced from the tabulations of De Wit and Arens[2], apparently taken at 20° C., and of Oakes[4], taken at 30° C. Levels of accuracy and of temperatures of observation are sufficiently close for points from the two sources to lie on a smooth curve. It also essentially includes the observations of Anderson and Low[3] throughout the range of their results.

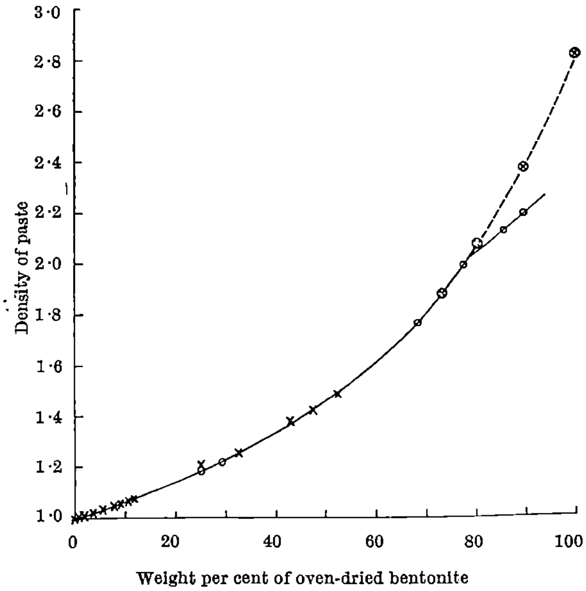

Fig. 1. Densities of Wyoming bentonite pastes. ×, Oakes's results; O, De Wit and Arens's results; ⊗, approximate positions of X-ray densities for the water contents at which the bentonites exhibit three, two and one layers of hydration water, and for the bare lamellæ. The dashed extrapolation indicates the trend which a curve would follow if no porosity were consequent to the shape of independent flakes

Montmorillonite, the main mineral constituent of bentonite, is abundantly documented as having a remarkable laminar structure in which individual laminæ are more or less independent. In the absence of an enveloping medium, the density of an aggregate of independent flakes makes up a fraction of the true density roughly comparable to the 91 per cent of a given volume which can be occupied by a packed set of equal disks. That is, the aggregate volume per disk is 110 per cent of the volume of a single disk. In an excess of enveloping medium, each lamina occupies only its own characteristic volume.

The unit dimensions, based on Pézerat and Méring's[5] X-ray measurement of parameters within layers, and the structural formula of montmorillonite in analysed Wyoming bentonite, afford a calculated density of 2·83 for the laminæ alone. This is in suitable agreement with the observed density of pyrophyllite, in which layers of nearly identical dimensions and compositions are not independent, and is about 1·1 times the 'density' measurements obtained from dry montmorillonite.

Table 1

Conc. wt. per cent oven-dry bentonite in paste	Density determination		Average specific volume of water	Apparent specific volume of bound water, if bound water equals 0·3 the weight of bentonite
	Oakes	De Wit and Arens		
0·000	0·99564	(0·998)	1·0044	
0·982	1·00155		1·0048	
1·795	1·00730		1·0044	
3·64	1·01950		1·0045	
5·35	1·03145		1·0044	
7·52	1·04594		1·0051	
8·70	1·05452		1·0050	
10·60	1·0687		1·0048	
11·42	1·0750		1·0047	
24·93		1·186	1·008	1·06
25·00	1·200		0·994*	
29·05		1·222	1·009	1·06
32·30	1·2572		1·0058	1·03
42·75	1·3719		1·0158	1·06
47·6	1·4241		1·019	1·06
52·4	1·4894		1·021	1·05
68·5		1·772	1·023	1·04
77·9		2·001	1·02	
85·75		2·134	1·16	
89·60		2·199	1·33	

* Note departure from curve in Fig. 1

In Table 1, apparent average specific volumes of water in the several pastes cited are arrived at by simple subtraction of the volumes of the montmorillonite laminæ present from the total volume.

It is also frequently inferred that montmorillonite laminæ rather strongly control up to about one-third of their own weight in water molecules (cf. Bradley[6]). If normal specific volume be assumed for the residue of water in these pastes which is not so controlled, the apparent specific volume of controlled water may be calculated and is listed for several cases in Table 1.

In Oakes's pastes the exchange base present was sodium ion, and it must be presumed that these ions were associated mainly with the bound fraction. Their abundance with respect to bound water is about 8 per cent by weight, or 2 per cent by volume. Allowance of 2 per cent positive error for each of the sodium ion paste entries still leaves an average of about 1·04 for the specific volume of the bound water.

The more elegant procedure of Anderson and Low[3] avoids the rather complicated assumptions outlined above by measuring the rate of change of volume of a paste as water is expressed from it. At the level of 62·5 per cent solids (Fig. 1), they found apparent specific volumes for the water being expressed of 1·02–1·03, in excellent agreement with the calculated volumes at comparable solid content in Table 1.

In the region 75 per cent solids (77 per cent if the estimate for bound water of 0·3 by weight of the solid were assumed to be a fixed quantity) the water becomes insufficient to constitute a continuous phase. Apparent specific volumes for water then lose their meaning, and the density determinations depart gradually from the smooth 'theoretical' curve toward the bulk density of packed solid disks. Instead of the 'apparent molar volumes' for the last two entries in Table 1, apparent porosities may be estimated, and they are about 3 per cent and about 6 per cent respectively. Apparent porosities for cited weighed oven-dried aggregates are about 10–15 per cent.

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[1] Mackenzie, R. C., *Nature*, 181, 334 (1958).

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DR. BRADLEY has very successfully correlated data from diverse fields of study to show the essential agreement in density determinations on montmorillonite pastes. In this connexion it is interesting to note that early determinations carried out at this Institute, and referred to previously[1], fall quite nicely on the spur of the curve above 77 per cent solids.

In considering the extrapolated part of the curve, however, it must be remembered that montmorillonite oven-dried even at 135° C. (as used by Oakes[2]) always contains some residual sorbed moisture (the amount may be a few per cent[3]), and hence it is rather surprising that Dr. Bradley's density value for dry montmorillonite (calculated from X-ray and chemical data) fits the curve so closely. One would have expected some slight discrepancy in view of the fact that the pastes involved were made up with oven-dry montmorillonite. A montmorillonite (Wyoming bentonite) for which we have X-ray and accurate chemical data[3] gives a calculated density of 2·78—somewhat lower than Dr. Bradley's value, and the true hypothetical value for 100 per cent oven-dry montmorillonite would be expected to be even lower. The value for dry montmorillonite is somewhat critical in estimating the specific volume of the 'bound' water and, furthermore, it might be remarked that the bulk specific volume of the 'bound' water would be expected to vary with the exchangeable ion and may not be the specific volume of all fractions of this water. One wonders, too, whether it would necessarily be expected that the extrapolated density : montmorillonite-concentration curve need be a smooth continuation of that obtained in the lower concentration regions.

In view of the difficulties in assessment of the final part of the curve (more than 77 per cent solids) there is, to my mind, as yet no unequivocal evidence from density measurements as to the configuration of the *first* amounts of water sorbed by montmorillonite.

The divergences in discussion mentioned by Dr. Bradley surely arise from the fact that different authors have been considering the interpretation of results from rather different points of view. In the lower solids-concentration region all are agreed that density measurements can give an overall estimate of the density of the water present, the essential accuracy of which is clearly demonstrated by the elegant experiments of Anderson and Low[4].

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[1] Mackenzie, R. C., *Nature*, 181, 334 (1958).

[2] Oakes, D. T., Proc. Fifth Nat. Conf. Clays and Clay Minerals, 46 (Nat. Acad. Sci.—Nat. Res. Council Pub. No. 556, 1958).

[3] Mackenzie, R. C., *Silic. Indust.* (in the press).

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Structure and Mode of Action of the Contact γ-Aluminium Oxide/Platinum

ON the hypothesis of the free-radical structure of heterogeneous catalysts[1,2], the mechanism of many catalytic reactions has been deduced in recent years[3]. In order to explain the action of the γ-aluminium oxide (Al_2O_3)/platinum contact, the structure of the radical γ-Al_2O_3 (ref. 4) as an active transient phase with structural defects should be considered. The model formula of the non-active oxide Al_2O_3 can be represented as follows : $O{=}Al{-}O{-}Al{=}O$. The active γ-Al_2O_3 contains the radicals : $O{=}Al{-}$ and $-O{-}Al{=}O$. Though this formula could be written in several similar forms, because Al_2O_3 is a macromolecular compound, only two types of radical can be expected, namely, $R{=}Al{-}$ (electron donor) and $R{=}Al{-}O{-}$ (electron acceptor).

Since the contact γ-aluminium oxide/platinum is obtained as a product of the action of chloroplatinic acid on active γ-aluminium oxide, there is a possibility of exchange between the two compounds, according to the equation :

$$(O{=}Al{-}\ \ {-}O{-}Al{=}O)_2 + 2H^+PtCl_6^{2-} \rightleftharpoons (O{=}Al{-}OH)_2 + 2(AlO)^+PtCl_6^{2-}$$

Under the influence of an excess of chloroplatinic acid, the dissociation of aluminium–platinum compound goes backwards; this can also be explained by the action of the active γ-aluminium oxide as a chromatographic column[5]. In the stream of hydrogen the undissociated $(AlO)_2PtCl_6$ undergoes reduction as follows :

$$(AlO)_2PtCl_6 + 3H_2 \rightarrow (O{=}Al{-})_2 + Pt + 6HCl$$

and as a result of this the radical $O{=}Al{-}$ appears, which is necessary as an important link in the chain of reactions leading to the hydrogenation of benzene. Thus the active γ-aluminium oxide acquires electron donor properties. But when the concentration of chloroplatinic acid is small, the complete suppression of the dissociation of $2(AlO)^+PtCl_6^{2-}$ is doubtful, this compound being able, under the influence of hydrogen, to retain its ionic form. This checks the regeneration of the primary radical $O{=}Al{-}$, according to the reaction :

$$2(AlO)^+PtCl_6^{2-} + 2H_2 \rightarrow 2(AlO)^+2Cl^- + 4HCl + Pt$$

This explains why γ-aluminium oxide/platinum contacts with small contents of platinum lose their activity quickly[6], because, in my opinion, in the absence of sufficient numbers of $O{=}Al{-}$ radicals, platinum only activates hydrogen so long as it is saturated with it or with a hydrogen compound (*cyclo*hexane) :

$$Pt + H_2 \rightarrow Pt/H + H$$

But when the radical $O{=}Al{-}$ appears and co-operates with metallic platinum, then platinum, passing into the atomic state, can also make use of the electrons of $O{=}Al{-}$ and of molecular hydrogen in turn, so that hydrogen is activated. In consequence of this the hydrogen electron, together with its proton, is as it were thrown aside after the electron arising from the $O{=}Al{-}$ radical becomes available, and so on in a constantly repeating rhythm[7]. The mechanism of the reaction of hydrogenation of benzene at the γ-aluminium oxide/platinum contact can be represented in the form of a chain reaction, which is accompanied by a migration of electrons[7].

$$O{=}Al{-} + Pt + H_2 \rightarrow O{=}Al{-} \ldots Pt \ldots H + H$$
$$3\,(O{=}Al{-} \ldots Pt \ldots H) + 3H + C_6H_6 \rightarrow C_6H_{12} + 3\,(O{=}Al{-} \ldots Pt), \text{etc.}$$

The γ-aluminium oxide/platinum contacts are prepared by mixing a suspension of the oxide with the solution of chloroplatinic acid; in consequence the acid is adsorbed on the surface of aluminium oxide. The method described by Trzebiatowski and Kubicka[6] produces less active catalyst than that of Kobozev and co-workers[8]. It should be made clear that in the first case the authors worked at a higher temperature-range of the mixture (on a water-bath), while in the second case all operations are carried out at room temperature. It is believed that the O=Al— radicals disappear more easily at higher temperatures, transforming themselves into cations $(AlO)^+$ according to the first reaction given above.

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[1] Krause, A., and Krach, H., *Ber. dtsch. chem. Ges.*, **69**, 2709 (1936). Krause, A., in Alexander's "Colloid Chemistry", **7**, 175 (New York, 1950).

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GEOLOGY and MINERALOGY

A Marine Transgression of Boreal Age in the Southernmost Part of Norway

IN the summer of 1956 the Quaternary history of a number of trough-shaped basins was investigated in the area between Lindesnes and Kristiansand. In one such basin, at Dostad in the innermost part of Hartmarkfjord (lat. 58° 02′ N., long. 7° 38′ E.), a mire was found at a depth of about 1·5 m., lying between layers of marine sediments (Fig. 1). The basin is very well sheltered from the sea by, among other things, a rock threshold which is about 2 m. above present sea-level. The mire is 1·5–1·7 m. thick.

A variation in the proportions of marine to freshwater diatoms was observed in the mire. The 50 cm. directly above the marine clay (*e*) and including the gyttja (*d*) contains only freshwater forms. Farther up, a few salt water forms appear together with freshwater species. The proportions of salt water forms increase upwards until at the top only marine forms are present.

The mire rests on marine clay and is covered by marine diatomaceous earth (quantities of *Melosira* (*Paralia*) *sulcata* and many *Navicula lyrata* types) on top. It seems probable that these diatoms have actually lived here.

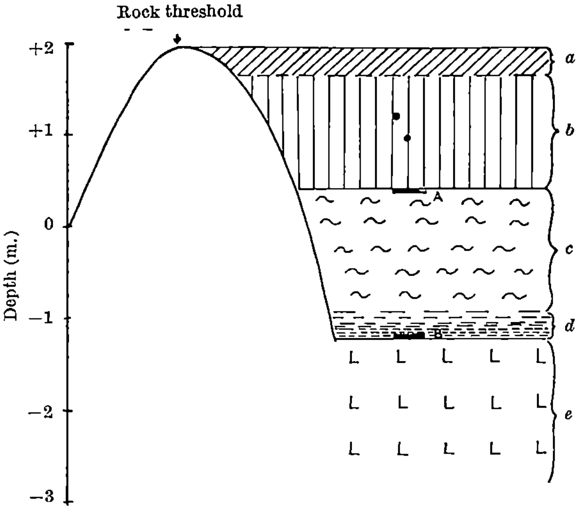

Fig. 1. Vertical scale exaggerated. *a*, Cultivated soil; *b*, marine diatomaceous earth; *c*, 'peat'; *d*, freshwater gyttja; *e*, marine clay

Samples were collected for pollen and diatom analyses by means of a Hiller peat sampler. Miss Kari Egede Larssen, of the Norwegian Geological Survey, has been kind enough to carry out pollen analyses of samples from the base and the top layers of the mire. Both samples contain considerable quantities of *Corylus* (15–17·5 per cent), but practically no *Alnus* pollen. In addition, many macroscopic fossils were found, among which were nuts and leaves of *Corylus* and tree branches. Miss Egede Larssen states that in all probability the samples are of boreal age.

For carbon-14 datings, horizontal slices of the 'peat' 2–3 cm. thick were collected. One was taken from the top of the mire and one from the bottom (Fig. 1, *A* and *B*). The datings have been carried out by the Radiological Dating Laboratory at the Norwegian Institute of Technology in Trondhjem. The ages of the samples were found to be 8,770 ± 100 years (B.P.) and 9,410 ± 220 years (B.P.) respectively.

This part of Fennoscandia is peripherically situated with respect to the rise of the land after the last Ice Age and the marine transgressions could occur because eustatic movements would easily be stronger than the isostatic movement.

Referring to the above-mentioned datings, one must accept that the Dostad basin was isolated from the sea because of a regression which occurred approximately 9,400 years ago. A rich vegetation came into existence and lasted until approximately 8,800 years ago, when a transgression of the sea, probably eustatic in origin, drowned this boreal vegetation.

Such a great amount of marine diatomaceous earth as was formed afterwards has, apparently, never previously been recorded in Norway. Marine diatomaceous earth has been observed in Sweden[1].

Several Swedish authors[2,3] have given diagrammatic representations of the movement of the shoreline in the Gothenburg area, and these show that a transgression began to make itself clearly apparent about 7000 B.C. One of these authors repeats this again in a later publication[4]. The "time of sinking of the land" must in any event have begun before *Alnus*, *Quercus* and *Tilia*, etc., appeared in the region[1] (northern Halland). Fromm is quoted[5] as having found, from the pollen analysis results of varved sediments, that the *Alnus* curve began about 6300 B.C. This dating is valid for southern Sweden. A great peat column at Adak in Northern Sweden has been dated by the carbon-14 method, thus placing the beginning of the *Alnus* curve at 6620±125 B.C.[5]. The pollen analysis from the upper part of the mire (Fig. 1,*c*) indicates that its age is apparently not far from the time when the *Alnus* curve began. This correlates very well with the radiological dating from Sweden.

Marine sediments resting directly upon a boreal terrestrial deposit have apparently not been previously reported in Norway. The occurrence of marine diatoms, as described above, indicates that sea-level was not far below the rock threshold and that waves were able to break over it, for example, during storms and exceptionally high-water levels. The minimum level of the boreal shore-line, judging by the evidence of the diatoms, was not far from the present sea-level in the area. However, work on a graph of the movement of the shore-line is being carried out at present, and more detailed results will be published later.

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[1] Halden, Bertil E., *Sverig. geol. Unders. Afh.*, Ser. C, No. 310 (1922).

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Olivine-Spinel Transformation

IN the light of A. E. Ringwood's recent synthesis of a spinel form of fayalite (private communication), Fe_2SiO_4 (the iron end-member of the fayalite–forsterite mixtures which comprise the bulk of natural olivines), it seemed worth while to attempt a synthesis of a spinel form of forsterite, Mg_2SiO_4. Ringwood prepared the fayalite-spinel at about 50 kilobars and 500° C., and his calculations indicated that the forsterite-spinel should become stable at about 100 kilobars and 500° C. It is possible that olivine is abundant in deeper layers of the Earth (50–1,000 km.) and hence some knowledge of its phase transitions would be of geological interest[1].

To study these possible phase transitions, appropriate mixtures of dry and hydrous oxides were loaded into a carbon capsule contained in a high-pressure, high-temperature apparatus. After the pressure on the capsule was increased to the desired level, it was electrically heated to about 550° C. for about 20 min. (Crystals of 10 or 20μ average diameter formed in 5 min.) Then the sample was quenched to room temperature and the pressure was reduced to atmospheric. In this way any phases formed at high pressure would tend to be preserved. Various hydrated phases formed if the maximum temperature did not exceed about 500° C.

Table 1

Charge	Pressure (kilobars)	Products identified
2 $Mg(OH)_2+SiO_2 \cdot nH_2O$	95–130	Forsterite
$Fe+Fe_3O_4+SiO_2 \cdot nH_2O$	110	Ringwood's fayalite-spinel (Debye–Scherrer patterns agree)
$Fe+Fe_3O_4+MgO+SiO_2 \cdot nH_2O$	110	Forsterite, fayalite-spinel
Hawaiian olivine	93–(hot)	Olivine melted and frozen this run. Olivine recovered
Moist Hawaiian olivine	90–110	Olivine unchanged
2 $Mg(OH)_2+0{\cdot}9\ SiO_2+0{\cdot}1\ GeO_2+H_2O$	110	Forsterite
2 $Mg(OH)_2+SiO_2 \cdot nH_2O$ +5 per cent Ni_2GeO_4	110	Forsterite
2 $NiO \cdot SiO_2 \cdot nH_2O$	90–110	Nickel forsterite (no spinel)
2 $ZnO \cdot SiO_2 \cdot nH_2O$	90	New phase, r.i. 1·78, biaxial. No spinel

Table 1 summarizes the results of these experiments.

Thus no other olivinic spinel other than Ringwood's fayalite-spinel formed in these experiments. Perhaps higher pressures are necessary. This work will be continued.

I am indebted to A. E. Ringwood and Prof. F. Birch for stimulating the work on this problem and for providing some of the oxide mixtures.

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[1] *Nature*, 178, 1303 (1956).

PALÆOMAGNETISM

Late Tertiary Geomagnetic Field in North-western Canada

THE fundamental assumption made in interpreting palæomagnetic results is that the average geomagnetic field corresponds to that of a central axial dipole. This communication reports on some palæomagnetic results which support this assumption and which were made on Late Tertiary volcanic rocks, which were collected during the summer of 1955 from north-western Canada by field geologists of the Geological Survey of Canada from flat-lying, undisturbed, vesicular basalts.

Forty-eight samples were collected from four different localities. The largest suite, twenty-nine amples, was collected by J. O. Wheeler from lavas exposed near Whitehorse, Yukon, at a latitude of 60·5° N. and longitude of 135·0° W. Another nine samples were collected by W. H. Poole near Wolf Lake, Yukon, at 60·0° N. and 130·5° W. L. H. Green collected six samples near Selkirk, Yukon, at 63·0° N. and 138·0° W., and J. D. Aitken collected four samples near Surprise Lake, British Columbia, at 59·5° N. and 134·0° W.

These samples were measured on a magnetometer of the rock generator type at the Geological Survey of Canada during 1958. The results of these measurements are shown in Fig. 1 on a stereographic projection, full and open circles representing north poles on the lower and upper hemispheres respectively. All the rocks collected by Wheeler and Green are reversely magnetized while the rest are normal except for two of Poole's samples, which are almost horizontally polarized.

The mean direction of these rock samples has been computed by reversing all the reversely polarized rocks and adding them to the normal ones. The two horizontally polarized samples are considered to be anomalous, due perhaps to magnetization caused by lightning, and have not been included in the statistical analysis. The mean direction, *H*, with its Fisher statistics, has been listed in Table 1, where it is compared with the field, *F*, produced by a central axial dipole and the present geomagnetic field, *F′*, at

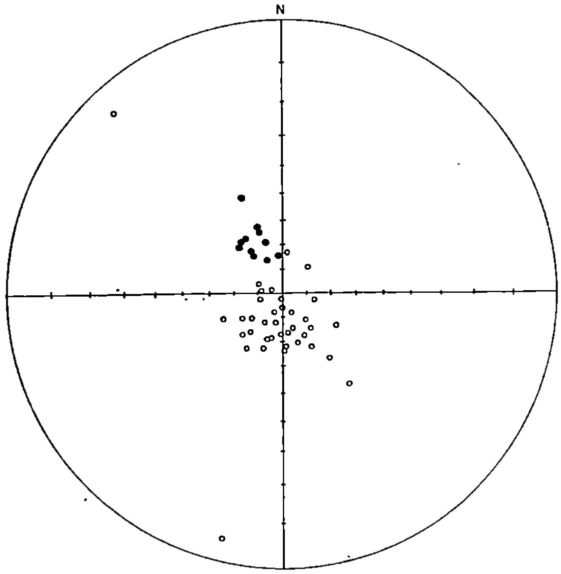

Fig. 1. Stereographic projection of palæomagnetic directions of Late Tertiary volcanics from north-western Canada. ●, North pole on lower hemisphere; ○, north pole on upper hemisphere

60·0° N. and 135·0° W. The λ's are the angles between the palæomagnetic direction, *H*, and *F* and *F′*.

Table 1 shows that the mean palæomagnetic direction of these Late Tertiary rocks is equivalent to the axial dipole field expected at this locality and is significantly different from the Earth's present field. These results are therefore further evidence to support the basic assumption of most geophysical interpretations of palæomagnetism, namely, the average magnetic field of the Earth is due to a geocentric axial dipole.

Table 1

	H	*F*	*F′*
D	348·5	0·0°	31·0°
I	+ 75·0	+ 74·0°	+ 76·0°
θ	4·0°	—	—
K	28·0	—	—
N	46	—	—
λ	0°	3·5°	10·5°

D, Declination east of north; *I*, inclination (+ north pole down); θ, angular radius of circle of confidence at 95 per cent level; *K*, Fisher's dispersion; *N*, number of samples.

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P. M. DU BOIS

Geological Survey of Canada,
Ottawa. Feb. 23.

PHYSICAL SCIENCES

Simultaneous Occurrence of Sub-Visual Auroræ and Radio Noise Bursts on 4·6 kc./s.

SINCE July 1958 the red oxygen (6300 A.) airglow has been recorded at Camden, near Sydney (geomagnetic latitude 42° S.), with a sky-scanning photometer. This instrument has been described by St. Amand[1]. These observations frequently detected greatly enhanced emission towards the south, and less often structures such as arcs and rays. We interpret these as auroræ, usually sub-visual, though on seven nights auroræ were seen.

Table 1. OCCURRENCE AND ABSENCE OF NOISE ON 4·6 KC./S. AND AURORÆ

		Noise on 4·6 kc./s.	
		Yes	No
Auroræ	Yes	18	2
	No	6	27

During the same period, radio noise on 4·6 kc./s. was continuously recorded by a method[2] which largely eliminates impulsive atmospheric and industrial interference. These observations[3] frequently detected distinct noise bursts, many times stronger than the background and usually lasting a few hours.

A comparison of the radio and nightglow records shows that there is a definite correlation between the two. Of 53 nights of simultaneous observations of noise and airglow between June and December 1958, noise bursts and sub-auroræ were recorded during the same hours on 18 nights. On 27 nights neither noise nor sub-auroræ were recorded; on 6 nights noise was recorded in the absence of any auroral pattern in the airglow, while on two occasions auroræ were recorded without any noise bursts. This is summarized in Table 1.

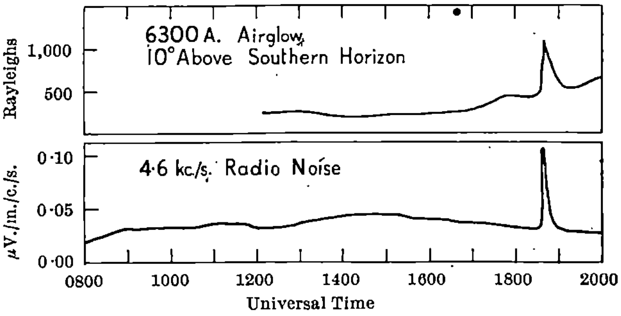

Fig. 1. Noise and auroral burst observed on July 21, 1958

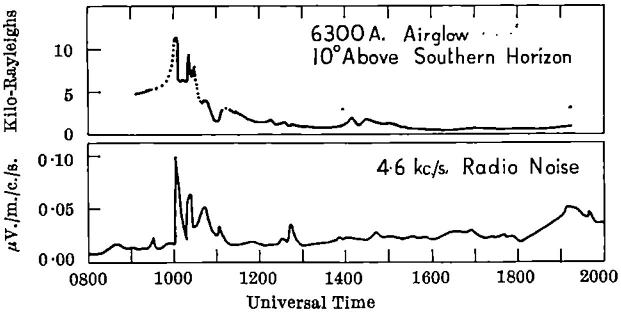

Fig. 2. Airglow and noise records for August 27, 1958. No red airglow observations were made during those periods for which the trace is dotted

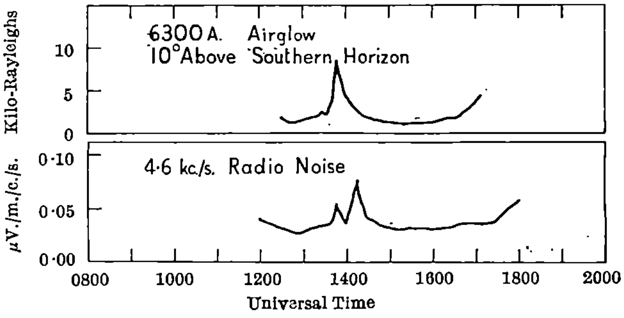

Fig. 3. Noise and airglow records for January 5, 1959

As might be expected, both phenomena are related to magnetic disturbance. They tend to occur when the disturbance index (K) reaches or exceeds 5.

On a few nights the fluctuations of noise and light intensities have shown a minute-to-minute correspondence (Figs. 1–3). This suggests that they may both be directly generated by the same phenomena, possibly the entry into the atmosphere of proton or electron streams.

However, there is in general no exact correspondence between the two; as Table 1 shows, one is occasionally observed without the other. The radio noise, unlike the auroral light, should be detectable even when its apparent source lies below the horizon. This probably accounts for much of the looseness in the association between the two, and for the occasional observations of noise without auroræ. However, the two cases of auroræ without accompanying radio noise cannot be explained in this manner. If the auroræ are caused by proton or electron streams, then it follows that such streams do not always generate radio noise.

This work forms part of the research programme of the Upper Atmosphere Section of the Commonwealth Scientific and Industrial Research Organization.

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Dual Pumping Speeds of Some Ionization Pumps

In recent years the phenomenon of ion pumping in ionization gauges has received widespread attention. Work in many laboratories has shown that in an ionization gauge, activated gas molecules interact with the glass walls of the tube and are removed from the gas phase at a rate depending largely upon the pumping history of the gauge. Alpert[1], Nottingham[2] and others have shown that in the Bayard–Alpert form of gauge, the glass walls assume an electrical potential, slightly negative with respect to the cathode delivering primary electrons, and the pumping action of the gauge is due largely to ions which acquire a high kinetic energy and are driven into the walls.

Comsa and Musa[3,4] have described an ion pump in which ions are collected by the glass walls alone—there is no specific ion collector in their tube—and have calculated that the glass walls acquire a potential, determined by the equality of electron and ion bombardment, about 5 V. negative with respect to the cathode. The pumping speed of such a tube was reported to be 0·03 l./sec./m.amp.

However, experiments performed during the past three years in these laboratories on Bayard–Alpert gauges have revealed that such gauges possess two distinct pumping speeds, one about five times the other, and it has been suggested[5,6] that the electrical potential of the inner surface of the glass walls, which, it has been proposed, assumes a value approximating to either cathode or anode potential, determines at which speed the gauge shall pump. Later work on a gauge of similar design to that of Comsa and Musa has shown that this type of gauge also possesses two distinct speeds and that the wall potential can assume either of the two aforementioned values.

The potential of the inner glass surface was measured by surrounding the gauge envelope with a metal sheath which was connected via any of a number of capacitors of known value to ground. The voltage appearing upon the sheath was applied to an electrometer amplifier. The approximate voltage on the inner glass surface was then deduced from a knowledge of the capacitance of the gauge-sheath system (approx. 50 pF. as measured with a similar tube and sheath).

These measurements showed that if the glass potential approximated to that of the cathode the gauge pumped relatively quickly, but if the potential was high ($\sim$ 200 V. in our estimation) there was only a slight pumping action. In this latter condition probably few ions could reach the walls. When the gauge had been outgassed for a short time only, soon after commencing experiments, it was found possible to control the wall potential. If the electron emission was initiated before applying anode potential, the walls become stabilized at cathode potential. If, however, anode potential was applied before activating the filament, the walls became charged positively. After a number of outgassing cycles (a total of about 10 hr. at 400° C.) had been performed it was observed that no control could be exercised over the wall potential, stabilization occurring at cathode potential only.

As pointed out by Comsa and Musa, the walls become stabilized at cathode potential when the primary electron and ion currents balance, but it is believed that a second stabilization potential occurs at which the primary electron current is balanced by a current of secondary electrons emitted from the glass[7] (at about 200 V. in our experiments). When the glass is comparatively new and contains much occluded gas, the second stabilization potential can be obtained since the secondary emission coefficient of the glass can exceed unity, so allowing a current balance. When the glass is well outgassed there is evidence[8,9] to show that this coefficient will fall and stabilization at the higher potential becomes impossible. It is probable that Comsa and Musa observed one pumping action only, since they always activated the filament before applying any accelerating potentials and their outgassing techniques were stringent.

In this work a dynamic vacuum system[5,10] has been used so that the gas pressure in the experimental tube ($1{\cdot}0 \times 10^{-5}$ mm. mercury of argon) remained constant. Subsequent desorption of the pumped gas by heating the gauge enabled an evaluation of the speeds of the gauge to be made. These were: (1) when the glass became stabilized at -5 V. (approximately cathode potential), speed, 0·0003 l./sec./m.amp.; (2) when the glass became stabilized at $+$ 200 V. (approximately anode potential), speed, 0·00005 l./sec./m.amp.

The rate of ionic bombardment of the walls was determined in a gauge which included a cylindrical ion collector close to the walls, and it was shown that the higher of the above speeds corresponds to an ion clean-up efficiency of about 10 per cent.

In conclusion, it can be stated that an ion pump of the design proposed by Cosma and Musa inherently possesses two pumping speeds and in the early stages of use of this pump, especially if the pump has not been well outgassed, either speed can be obtained by a suitable electrode potential switching sequence. The duality of pumping speeds has been found to be a result of charging of the glass walls to either approximately cathode or anode potential.

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April 6.

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Evidence for a Variable Long-range Order in Nearly Anhydrous Gamma Alumina

THE nature of the cubic or nearly cubic alumina called γ- or η-Al_2O_3 has been the subject of much speculation. Its structural similarity to the spinels has been known for many years[1–3] and led to the view that γ-Al_2O_3 is a defect structure which can be written $Al_{21\frac{1}{3}}\square_{2\frac{2}{3}}O_{32}$ with 21⅓ aluminium ions occupying statistically 24 cation sites in the spinel structure.

The recognition that γ-Al_2O_3 is frequently not a fully dehydrated alumina led de Boer and Houben[4] to suggest that 'water' may be an integral part of the structure and that an ideal formula may be $H\,Al_5O_8$ analogous to the spinels $Li\,Al_5O_8$ and $Li\,Fe_5O_8$ (see ref. 5). In these structures the lithium ions occupy particular positions in the lattice and therefore one might expect that if γ-Al_2O_3 is really $H\,Al_5O_8$, the hydrogen ions (or more likely the OH ions) likewise will occupy particular positions.

Saalfeld[6] has discussed the dehydration of gibbsite to boehmite and the subsequent formation of a nearly anhydrous alumina. The reactions are orderly in a crystallographic sense and the resulting γ-alumina is shown to be tetragonal with $a = b = 7{\cdot}95$ A. and $c = 7{\cdot}79$ A. We have found confirmation of this result in the course of studying the dehydration kinetics of a well-crystallized gibbsite. The nearly anhydrous alumina yielded a double peak in the position of the strong (400) spinel reflexion with components $d = 1{\cdot}98$ and $1{\cdot}95$ A. The longer spacing gives the more intense reflexion and corresponds to (400) and (040) with $a = b = 7{\cdot}96$ A. and the shorter spacing corresponds to (004) with $c = 7{\cdot}80$ A.

One may reasonably surmise that if dehydration occurs slowly from well-crystallized material, the ordered tetragonal structure is formed. This appears to be the γ-alumina of Stumpf[7] and Russell[8]. When dehydration takes place in a less orderly manner or from less favourable starting materials, then a statistically cubic material is formed which gives the spinel-type X-ray pattern.

We have obtained additional evidence for structural order in nearly anhydrous alumina prepared by slow dehydration of gibbsite. When the dehydration is carried beyond about 90 per cent of completion, a long spacing of the order of 30–90 A. is reproducibly formed and is fairly stable to atmospheric conditions. The peak occurs in the region of $2\theta = 1$–$2°$, with copper $K\alpha$ radiation. The peak is observed first at about 80 per cent of complete dehydration but at this stage some boehmite still remains. Fig. 1 shows plots of diffracted intensity against 2θ and it is obvious that, as dehydration goes to completion, the diffraction peak moves to smaller 2θ values and finally is lost in the direct beam. Usually only one peak is observed, occasionally two can be observed, so that the long-range order arising from the residual 'water' is of a statistical character. The well-defined peaks shown in Fig. 1 were obtained by 12-hr. heat-treatments at successively higher temperatures up to about 500° C. Dehydration carried out directly at 450–500° C. gave poorer peaks, though they still occurred.

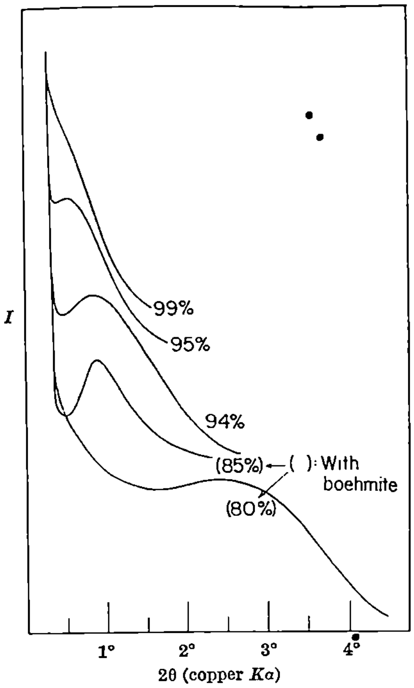

Fig. 1. Small-angle X-ray diffracted intensity from nearly anhydrous gamma-aluminas prepared from gibbsite. The percentage dehydration of the gibbsite is given for each curve. Note, however, that for 80 and 85 per cent dehydration, the remaining water is contained partly in residual boehmite

In terms of oxides, the ideal formula $H\,Al_5O_8$ is $Al_2O_3.\frac{1}{5}H_2O$ and corresponds to one-fifteenth of the initial 'water' content, that is, 6·7 or 93·3 per cent of complete dehydration, and the corresponding long spacing in Fig. 1 is about 65 A.

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FORTHCOMING EVENTS

*(Meeting marked with an asterisk * is open to the public)*

Monday, June 8

Royal Geographical Society (at 1 Kensington Gore, London, S.W.7), at 8.30 p.m.—Captain M. E. B. Banks, M.B.E.: "The Ascent of Rakaposhi".

Tuesday, June 9

Zoological Society of London (at the Zoological Gardens, Regent's Park, London, N.W.1), at 5 p.m.—Scientific Papers.

University of London (at the Institute of Archæology, Inner Circle, Regent's Park, London, N.W.1), at 6 p.m.—Mr. S. S. Frere: "Animals in the Roman Empire".* (Last of six lectures on "Animals in Archæology".)

Tuesday, June 9—Thursday, June 11

National Physical Laboratory (at Teddington, Middlesex)—International Symposium on "Interferometry".

Wednesday, June 10

Commonwealth Fruits Council (joint meeting with the Food Group of the Society of Chemical Industry and the National Farmers' Union, at the Royal Commonwealth Society, 18 Northumberland Avenue, London, W.C.2), at 10 a.m.—Meeting on "The Utilization of Apples and Citrus Fruits".

Institute of Information Scientists (at the Shaftesbury Hotel, Monmouth Street, London, W.C.2), at 6 p.m.—Annual General Meeting. 7.15 p.m.—Dr. Alexander King: "The International Development of Scientific and Technical Information Services".

British Psychological Society, Social Psychology Section (in Room 425, Birkbeck College, Malet Street, London, W.C.1), at 8 p.m.—Mr. L. T. Wilkins: "Some Aspects of Research Strategy in the Field of Delinquency".

Royal Institution (at 21 Albemarle Street, London, W.1), at 9 p.m.—Prof. R. S. Nyholm, F.R.S.: "Colour in Inorganic Chemistry".

Thursday, June 11

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. C. M. P. Johnson, Mr. G. A. Jones, Mr. W. R. Phillips and Prof. D. H. Wilkinson, F.R.S.: "A Study of the Levels in ^{19}F Following the Beta Decay of ^{19}O"; Mr. P. Dagley, Mr. M. A. Grace, Mr. J. M. Gregory and Mr. J. S. Hill: "Nuclear Alinement of Manganese-56".

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Lecturer in Physics—The Secretary, The University, 38 North Bailey, Durham (June 12).

Chief Agricultural Research Officer (with a first- or second-class honours degree in natural science or agricultural science, considerable research experience in tropical agriculture, and an aptitude for the direction of research) with the Government of Western Nigeria, to plan, organize and develop the work of the Research Division of the Ministry of Agriculture and Natural Resources, assist in the formulation of a crop research policy, and to advise the Agricultural Extension Services of the Region on the application of research findings to crop production problems—The Official Secretary (Recruitment Branch), Office of the Commissioner for Western Nigeria, 178/202 Great Portland Street, London, W.1 (June 13).

Lecturer in Chemical Engineering—The Registrar, University College, Singleton Park, Swansea (June 15).

Lecturer (with veterinary qualifications and postgraduate research experience) in Animal Health in the Biochemistry and Nutrition Section of the Department of Agricultural Chemistry—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (June 15).

Research Assistant (preferably with a knowledge of vacuum techniques or infra-red detectors) in the Department of Physics for work in the Optic Group on problems connected with the construction of filters for the infra-red region above 5 microns in wavelength—The Registrar, The University, Manchester 13 (June 15).

Tutorial Students in the Departments of Botany, Civil Engineering, Geology, Mathematics, Physics and Zoology—The Registrar, King's College, Strand, London, W.C.2 (June 15).

Scientific Officer or Senior Scientific Officer (male graduate with a first- or second-class honours degree in chemistry, and preferably with some postgraduate experience) in the Department of Spectrochemistry, for duties covering various aspects of emission spectrochemical analysis and trace element investigations—The Secretary, Macaulay Institute for Soil Research, Craigiebuckler, Aberdeen (June 16).

Assistant Lecturer, and a Temporary Lecturer (medically qualified and preferably with experience in clinical bacteriology or virology) in the Department of Bacteriology—The Registrar, The University, Manchester (June 20).

Assistant Lecturer, Grade III (preferably with special qualifications and interests in plant physiology and biochemistry) in Botany—The Registrar, The University, Bristol 8 (June 20).

Demonstrator (preferably with an interest in histochemical or physiological aspects of comparative endocrinology) in Zoology—The Registrar, The University, Nottingham (June 20).

Junior Research Fellow in Pure Mathematics—The Registrar, The University, Sheffield (June 20).

Lecturer or Assistant Lecturer in Applied Mathematics—The Registrar, The University, Southampton (June 20).

Lecturer (with practical experience in the aircraft industry and preferably some research experience) in Aircraft Structures in the Department of Civil Engineering—The Registrar, The University, Leeds 2 (June 20).

Lecturer in Chemistry, and a Junior Lecturer in Biochemistry—The Secretary, Medical College of St. Bartholomew's Hospital, West Smithfield, London, E.C.1 (June 22).

Research Assistant in the Department of Botany, for research on physiological genetics using tissue culture techniques—The Secretary, University College, Gower Street, London, W.C.1 (June 22).

Research Assistant (with a good honours degree, a knowledge of French and German and the ability to draw maps) in the Department of Geography—The Registrar, The University, Leeds 2 (June 22).

Junior Fellow (with a university degree) in the Department of Veterinary Surgery—The Registrar, The University, Bristol 8 (June 26).

Assistant in Mathematics—The Secretary of University Court, The University, Glasgow (June 27).

Lecturer or Assistant Lecturer in Applied Mathematics—The Registrar, The University, Hull (June 27).

Lecturer or Assistant Lecturer (with special interests in organic chemistry) in Chemistry—The Registrar, The University, Sheffield (June 27).

Lecturer (with a medical qualification) in Bacteriology at the Royal Infirmary, Glasgow—Joint Clerk to the University Court, The University, Glasgow (June 27).

Research Fellow in Mathematics—The Secretary of University Court, The University, Glasgow (June 27).

Chair of Education in the University of Malaya—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (June 30).

Demonstrator in the Department of Organic Chemistry—The Registrar, The University, Leeds 2 (June 30).

Lecturer in the Department of Clinical Tropical Medicine—The Dean, London School of Hygiene and Tropical Medicine (University of London), Keppel Street, Gower Street, London, W.C.1 (June 30).

Lecturer or Assistant Lecturer in Organic Chemistry—The Registrar, The University, Leeds 2 (June 30).

Research Worker (with either an ordinary B.Sc. in chemistry and some knowledge of extraction and degradation of complex organic compounds or an honours B.Sc. with emphasis on natural products) in the Departments of Organic Chemistry and Botany, to aid an investigation into organic constituents of soils—The Registrar, The University, Liverpool (June 30).

Lecturer in Biochemistry at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 31).

Senior Lecturer (preferably with a sound knowledge of descriptive and/or experimental vertebrate embryology) in Zoology—The Registrar, University of Stellenbosch, South Africa (July 31).

Assistant Lecturer (with special qualifications in applied mathematics) in Mathematics—The Registrar (Room 22, O.R.B.), The University, Reading.

Assistant Librarian (Chartered Librarian, preferably with a working knowledge of German)—The Establishments Officer, Zoological Society of London, Regent's Park, London, N.W.1.

Fisheries Officer (with a university degree in biology with emphasis on zoology and experience of fisheries work) in the Northern Region of Nigeria, to execute plans for the development of river fisheries and the demonstration and organization of peasant fish culture—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.65/408/01.

Instructor or Assistant Professor in Protozoology—Dr. James R. Adams, Department of Zoology, University of British Columbia, Vancouver, B.C., Canada.

Junior Research Fellow in Mathematical Statistics—The Registrar, The University, Leicester.

Lecturer (with a good background in physics or chemistry with experience of research, as supervision of student thesis work is involved) in Plastics, and non-metallic materials generally, in the Department of Aircraft Materials—The Recorder, The College of Aeronautics, Cranfield, Bletchley, Bucks.

Master to teach Mathematics at all stages of the School, including the Sixth Form—The Headmaster, Boston Grammar School, Boston, Lincs.

Master to teach Physics up to at least first-year sixth standard—The Headmaster, King's College School, Wimbledon, London, S.W.19.

Professor of Physics at the University College, Colombo—The Ministry of Labour and National Service (E.9), 26–28 King Street, London, S.W.1, quoting E.9/72/TCS/CEY.

Reader in the Department of Electrical Engineering—The Registrar, Royal Technical College, Salford 5.

Research Biochemist (Ph.D. or Ph.D. candidate), for work on pyrimidine metabolism—Dr. Arnold H. Schein, Department of Biochemistry, University of Vermont College of Medicine, Burlington, Vermont, U.S.A.

Senior Lecturer (with a good honours degree in zoology and preferably a special interest in either entomology or physiology) in Zoology—The Secretary, Sir John Cass College, Jewry Street, London, E.C.3.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Overseas Information Services. Pp. 8. (Cmnd 685). (London: H.M. Stationery Office, 1959.) 6*d*. net. [43

Some Properties of Wiggin Electrical Resistance Materials. Pp. 36. (London: Henry Wiggin and Co., Ltd., 1959.) [43

The Royal Society and Nuffield Foundation Commonwealth Bursaries Scheme. Fifth Annual Report. Pp. 8. (London: Royal Society and Nuffield Foundation, 1959.) [43

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The Bedfordshire Naturalist, No. 12. (Journal of the Bedfordshire Natural History Society and Field Club for the year 1957.) Pp. 50. (Bedford: Bedfordshire Natural History Society and Field Club, 1959.) 5*s*. [53

General Register Office. Census 1951: England and Wales. Fertility Report. Pp. cxi+251. (London: H.M. Stationery Office, 1959.) 90*s*. net. [53

Department of Scientific and Industrial Research. The Investigation of Atmospheric Pollution: Research and Observations in the year ended 31st March, 1957. (Thirtieth Report.) Pp. iv+136. (London: H.M. Stationery Office, 1959.) 7*s*. 6*d*. net. [53

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Ministry of Housing and Local Government and Scottish Office. The Surface Water Year-Book of Great Britain 1956–57: Hydrometric Statistics for British Rivers, together with related Rainfalls for the year ended 30th September, 1957. Pp. xii+66. (London: H.M. Stationery Office, 1959.) 15*s*. net. [63

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The Development of Experimental Botany. By Prof. C. P. Whittingham. (An Inaugural Lecture given on March 11, 1959.) Pp. 15. (London: Queen Mary College, University of London, 1959.) [123

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B.B.C. Engineering Monograph No. 24: The Measurement of Random Noise in the Presence of a Television Signal. By L. E. Weaver. Pp. 16. (London: British Broadcasting Corporation, 1959.) 5*s*. [123

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United States Department of the Interior: Geological Survey. Bulletin 1042-N: Geology of Part of the Townsend Valley, Broadwater and Jefferson Counties, Montana. By V. L. Freeman, E. T. Ruppel and M. R. Klepper. Pp. iv+481–556+plates 42–46. n.p. Bulletin 1042-Q: Pegmatites of the Middletown Area, Connecticut. By Frederick Stugard, Jr. Pp. iv+613–683+plates 56 and 57. n.p. Bulletin 1046–O: Reconnaissance for Radioactivity in the Metal-Mining Districts of the San Juan Mountains, Colorado. By C. T. Pierson, W. F. Weeks and F. J. Kleinhampl. Pp. iv+385–413+plates 43 and 44 n.p. Bulletin 1061-E: Vegetation of Northwestern North America as an Aid in Interpretation of Geologic Data. By Robert S. Sigafoos. Pp. iii+165–185+plates 9–13. 75 cents. Bulletin 1064: Systematic Mineralogy of Uranium and Thorium. By Clifford Frondel. Pp. viii+400+plate 1. 1.50 dollars. Bulletin 1072–B: Barite Resources of the United States. By Donald A. Brobst. Pp. iv+67–130+plate 1. 40 cents. Bulletin 1086–C: Geophysical Abstracts, 174 (July–September 1958.) By Dorothy B. Vitaliano, S. T. Vesselowsky and others. Pp. iii+207–326. 35 cents. (Washington, D.C.: Government Printing Office, 1958.) [33

United States Department of the Interior: Geological Survey. Professional Paper 305–E: Test Well, Grandstand Area, Alaska. By Florence M. Robinson. With Micropaleontologic Study of Grandstand Test Well 1, Northern Alaska. By Harlan R. Bergquist. Exploration of Naval Petroleum Reserve No. 4 and adjacent Areas, Northern Alaska, 1944–53. Part 5: Subsurface Geology and Engineering Data. Pp. iii+317–339+plates 19 and 20. n.p. Professional Paper 305–F: Test Wells, Meade and Kaolak Areas, Alaska. By Florence Rucker Collins. With Micropaleontology of Meade Test Well 1 and Kaolak Test Well 1, Northern Alaska. Exploration of Naval Petroleum Reserve No. 4 and adjacent Areas, Northern Alaska, 1944–53. Part 5: Subsurface Geology and Engineering Data. Pp. iii+341–376+plates 21 and 22. n.p. Professional Paper 314–D: Geochemistry of Uranium in Apatite and Phosphorite. By Z. S. Altschuler, R. S. Clarke, Jr., and E. J. Young. Pp. iv+45–90+plates 11–13. 60 cents. (Washington, D.C.: Government Printing Office, 1958.) [33

Digging Into History: a Brief Account of Fifteen Years of Archaeological Work in New Mexico. By Paul S. Martin. (Chicago Natural History Museum—Popular Series, Anthropology, No. 38.) Pp. 157. (Chicago: Chicago Natural History Museum, 1959.) 1.50 dollars. [43

Canada: Department of Mines and Technical Surveys. Geological Survey of Canada. Bulletin 44: Structural Conditions in Canadian Coal Mines. By D K. Norris. Pp. 54+2 plates. 75 cents. Economic Geology Series No 18: Niobium (Columbium) Deposits of Canada. By Robert B. Rowe. Pp. vii+108. 75 cents. Memoir 297: Truro Map-Area, Colchester and Hants Counties, Nova Scotia. By I. M. Stevenson. Pp. viii+124+6 plates. 75 cents. (Ottawa: Queen's Printer, 1958.) [43

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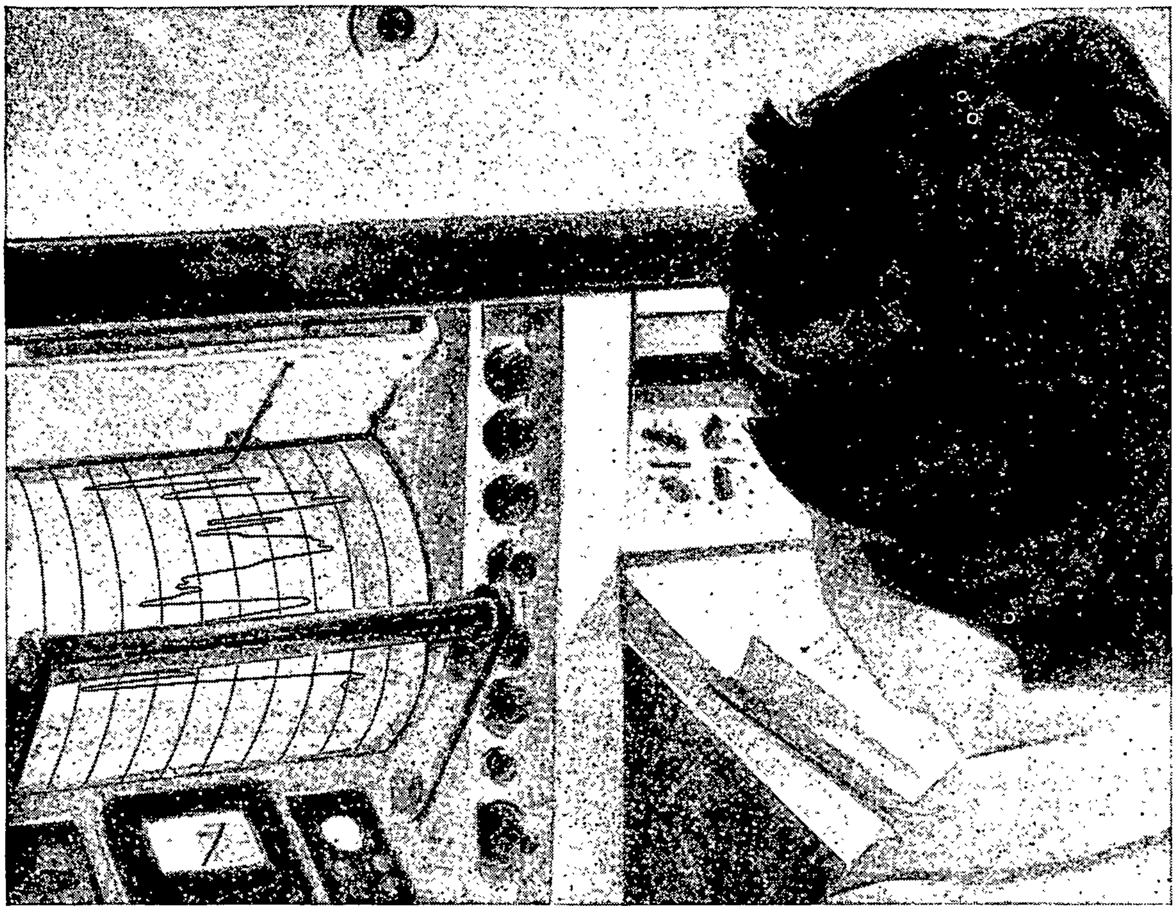

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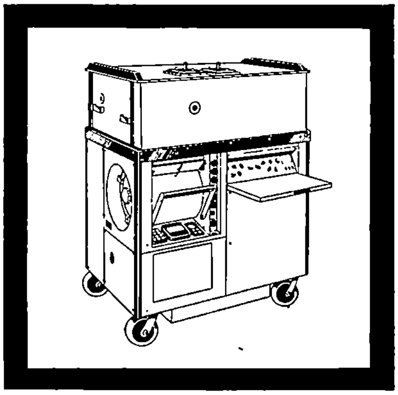

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TEACHING IN THE UNIVERSITIES

THE main functions of a university can be simply set down. There is the need to discover and interpret new knowledge; to impart knowledge and its interpretation to students; and to inspire them so that they will wish to join in the search for new truths themselves. In all that is done, the importance of imparting knowledge and understanding is pre-eminent. It is often wise to reflect how far this is successfully accomplished.

The university teacher has many critics; but those who are bad and beyond redemption are not nearly so many as the critics would have us believe. They are probably equal in number to those men and women who are naturally good lecturers and seem to have been born for the job. The large majority of university teachers are reasonably good craftsmen, sometimes aware of their deficiencies, conscious that their lectures frequently fail to impress, and whose shortcomings could be put right if they were prepared to spend some time learning their craft. They would get considerable help if they followed some of the advice put forward by G. Kitson Clark, reader in constitutional history in the University of Cambridge, and Commander E. Bidder Clark, who has had considerable experience with the use of visual aids to teaching in civil defence classes*.

As universities get bigger the problem of providing adequate and competent teaching staffs will become more and more acute. With increase in scientific and technological knowledge, the need for skilful exposition to promote real understanding will become more difficult, will require staffs prepared to make themselves good lecturers and who are prepared to use all the aids available to make their subjects intelligible.

The situation confronting a university lecturer is that confronting all lecturers. He must watch his audience to see that they are hearing and understanding him and that he is going neither too fast nor too slow. Yet how many lecturers find their inspiration on the ceiling, on the floor, or by the light of the windows: the students need not be present.

Nor should the lecturer be content with transmitting what is in his notes to the notebook of the student who, be he diligent, later returns them to the lecturer at an examination. The lecturer should seek to transmit what is in his mind to the mind of the student. This he will not do unless he periodically introduces checks to ascertain what is happening to the student's mind. A little acquaintance with the principles of pedagogy would help him considerably in practice.

For convenience, methods of instruction can be grouped into three. There is the straight lecture in which one voice alone is heard and which is particularly suitable for large classes. There is the discussion method in which a leader seeks to draw out and synthesize the combined knowledge and wisdom of a group. Then there is the 'lesson' method, so well developed in our schools, in which, by question and answer, the teacher uses an analytical method to develop knowledge and understanding in his pupil's mind. The tutorial class, so long an established feature at some universities, makes use of all three methods of instruction. The introduction of some questions and discussion would greatly improve the quality of many 'lectures', especially in science and technology, where the lecturer's voice is often broken only by the scratching of pens on paper.

Before a lecture begins, the teacher should consider his aims. As Kitson Clark and Bidder Clark write: he is there to serve his audience and should think of himself the whole time as "teaching *them*, interesting *them*, and giving *them* what they require, and can take". There is a limit to what men and women can digest in an hour, and too much produced too quickly in too complicated a fashion will leave them mystified and unsatisfied. The lecturer should aim at getting home a limited number of points, well defined, properly emphasized and arranged in some sort of logical order rather than in providing a running commentary or long stretches of narrative from which nothing stands out. Too often lecturers preparing their first course greatly exaggerate the amount that they will be able to cover in an hour as well as the amount of detail that they can deal with.

In general, the larger the class the slower the lecturer should go. The good lecturer, however, adapts himself to conditions which reveal themselves in the class-room itself.

The advice given by Kitson Clark is severely practical and contains hints as to how the lecturer should deliver his lecture. He suggests that the lecture should be divided into sections so that the lecturer may keep an eye on the clock and, if a section is taking up too much time, reduce it or cut it out altogether. The lecturer should take the class into his confidence and they should be told how he intends to arrange the course. A class which does not know where a particular lecture fits into a course will soon lose interest; and if, as some do, the lecturer conveys the impression that the course is not very important and rather uninteresting, he may not only lose the attention of the class but also their persons as well.

Many people find it a strain to listen too long to a lecture presented wholly in abstract terms. A lecture should be relieved from time to time by something concrete, a story used as illustration, a piece of narrative, or a striking fact which clinches some argument and makes it memorable; illustrations should be subordinated to the general purpose of the lecture.

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* The Art of Lecturing: Some Practical Suggestions. By Dr. G. Kitson Clark and Commander E. Bidder Clark, O.B.E. Enlarged edition. Pp. 41. (Cambridge: W. Heffer and Sons, Ltd., 1959.) 3*s*. 6*d*. net.

The successful lecturer never under-rates his hearers' knowledge or under-estimates their intelligence. He does not talk down to them—a matter of judgment and of sensitivity which grows from careful and continuous observation of their reactions during the course of a lecture. Above all, and this is probably the greatest fault with the majority of bad lecturers, he does not give the class at any time information which is readily obtainable from standard text-books. It is a sad commentary on university teaching that many students leave having read little more than the notes provided by their lecturers; the use of books as guides and friends is something they have to acquire much later.

The lecturer should consider his own physical position when he lectures. He should look at the class the whole time, and will be more effective if he stands rather than sits. If he stands he should always check his mileage; some lecturers travel surprising distances in an hour. (One famous 'walker' was estimated to have covered five miles during a striking lecture on the ketones.) Too much restlessness, manipulative tricks with one's gown, balancing on the edge of the rostrum, are disturbing and fidgeting to a class; the mouth should remain visible.

Some of Kitson Clark's most useful advice concerns voice production. Speaking at a wall from about 5 ft. off and cupping one's ears with one's hands gives a good idea of the effect on an audience. A lecturer should speak up with his head well up; shouting is less easy to hear than a comparatively soft voice with the words properly enunciated. A higher pitched voice is more easy to hear, but a lower pitched voice is more agreeable to listen to. As a lecturer becomes preoccupied or fatigued the voice tends to work up to a high note, sounding unpleasant and strained. This is more common in women than men; sometimes they inadvertently "sound aggrieved or lachrymose because their voices have got out of control".

It goes without saying that no lecture will be successfully presented unless it has been thoroughly prepared; one wit has argued that all good lectures are given the night before. Other matters which the lecturer should consider are the use to which he will put his notes, whether or not he expects his class to take notes, and the form they will take, and positive recommendations about books.

The case for the use of visual or aural aids to learning needs no arguing. Yet it is still surprising how little or badly they are used. The blackboard is a much-abused instrument which is seldom used to full advantage. Previous preparation of maps or diagrams in invisible (purple) chalk is of great help to the lecturer unskilled in cartography; a chalk broken before use saves many nerve-rending squeaks, especially if it is held at an angle of 45° to the board. Bidder Clark describes the contributions to better learning made by the blanket board, the prepared 'chart', models, the episcope and the film projector. These are well known but frequently little used because of the extra trouble involved in preparation and in manipulation during the lecture. The lecturer who is most concerned with teaching his class will undertake the additional preparation required and will always be welcomed by his class.

The fact that some university lecturers approach their teaching with the dilettante air of the amateur bewilders many students who have been brought up to expect high standards and find the change from school to university somewhat disturbing. They ask themselves why this should be so in institutions which are adorned by institutes and departments of education. Are university teachers unable to profit from courses on pedagogy? This is a matter which should be carefully considered by vice-chancellors and principals, particularly in the light of the Willis Jackson Report on the Supply and Training of Technical Teachers. The position could well arise that, in future, students taking Diploma in Technology courses at senior technical institutions may be better taught and acquire greater depth of understanding of their subjects than students taught by the all-too-prevalent lecturing method so widely used in British universities.

MAN AND THE UNIVERSE

The Individual and the Universe

By Prof. A. C. B. Lovell. (B.B.C. Reith Lectures, 1958.) Pp. vii+111. (London: Oxford University Press, 1959.) 10*s*. 6*d*. net.

ONLY those who have actually been confronted with the task of giving a series of broadcast lectures on such a subject as "The Universe" can fully appreciate the difficulty of the assignment: the Reith Lectures particularly so, for with these it is expected that the speaker will go beyond the mere science and say something about the social, political, and even religious implications of his subject. Moreover he is cut off from any easy reliance on the developed language of science, faced as he is by an audience spanning the whole population and ranging from mentally unskilled everymen to hypercritical scientists who tend to frown on such excursions by their colleagues into the popular realm. These latter may be right from some points of view, and it may well be useless pandering to the curiosity of the man in the street by telling him at his own level about the latest developments in science, but as with most lecturing it is the lecturer that profits most, and I imagine that Prof. Lovell will agree that such a public performance can be a thrilling and salutary exercise.

I have to confess that it is beyond my comprehension why it should be that the problem of the expansion of the universe should be singled out above other problems of science to become strongly associated not only in the popular mind but also in that of philosophers and even scientists with religious and ethical matters. Although the interior of the Earth is a good deal less accessible to direct observation than are the remoter parts of the universe, yet people would laugh if some well-meaning geophysicist were to lecture on "The Individual and the Inside of the Earth". But the Reith lecturer must deal with his audience as he finds it, and Prof. Lovell is to be congratulated on this masterly presentation of a fascinating account of the epic struggles that scientists are now making to understand this mysterious universe. As effective owner of the world's largest telescope, Prof. Lovell naturally tends to lay emphasis on the importance of fabulously expensive equipment for solving these major problems, but unless strongly supported at every stage by theory, and the intelligent imagination needed to develop it, the meaning of the messages produced by such equipment will not always emerge. The encouragement of originality of thought, with the conflicts this involves, is perhaps the main social problem of science in our time or any other time so far, as Prof. Lovell is at pains to bring out in his talks.

The theories so far developed to account for the expansion of the universe, described herein, illustrate how easily theory can slip over into metaphysics. The 'big-bang' exploding super-atom hypothesis, with its attempt to 'explain' the expansion by postulating far less known things, seems to me reminiscent of Huygens' rarefied medium moving round the Earth with great velocity, introduced to 'explain' gravitation, when what is always wanted is a workable theoretical structure that can enable predictions to be made. My own feeling is that there is some major element still missing in our appreciation of this whole problem, and I would venture to predict that until some new theoretical approach on less mystical lines than hitherto is forthcoming, no serious progress with the problem will occur however large a telescope we or others build—mainly it seems at present, according to Prof. Lovell, to impress the neighbours. Nature seldom yields her secrets to this sort of wooing, but prefers the subtler approach.

I believe that the continued creation and maintenance of the universe will eventually seem as natural and intelligible by means of theory (yet to be established) as the view that the Earth is round seems natural and intelligible on gravitational theory, and that in such an attitude lies the only hope of solving this or indeed any other problem. Even though at present it seeems difficult compared with problems already solved, there are not the smallest grounds for suspecting that its solution is destined to remain for ever beyond the range of man's intelligence and inventiveness. And this spirit of hopefulness for scientific method is the main message that pervades Prof. Lovell's enthralling lectures.

R. A. Lyttleton

CAMBRIDGE ANTHROPOLOGY

The Developmental Cycle in Domestic Groups

Edited by Dr. Jack Goody. (Cambridge Papers in Social Anthropology, No. 1.) Pp. vii + 145. (Cambridge: At the University Press, 1958. Published for the Department of Archæology and Anthropology.) 21*s*. net.

THIS is the first in a projected series of symposia in social anthropology, each to be devoted to essays by Cambridge anthropologists on a particular theoretical topic. The theme of this issue is the changing form and significance of the domestic group during its development, and the analytical use of taking this process into account.

The volume comprises an introduction by Prof. Fortes and four papers, three of which are based on field research by their authors. Freeman, in a characteristically thorough ethnographic description, deals with the formation and partition of the family among the Iban of Borneo: his essay is of especial value in that they reckon descent cognatically, a widespread mode of relationship the theoretical interest of which has been obscured by an almost exclusive concern of anthropologists with lineal descent systems. Goody correlates differences in social groupings and processes of production with variant rules of inheritance in West Africa. Stenning relates the composition and stability of the pastoral Fulani domestic group to the herd on which it depends, and incidentally gives some information on a highly interesting dyadic system of symbolic classification. The concluding essay, not based on field research but an analysis of Trobriand data, is a brilliant demolition by Leach of Malinowski's assumption that the different and apparently conflicting meanings of the word *tabu* are unrelated homonyms. This theoretical exercise is related to the volume's theme mainly in its consideration of the significance of the change of a Trobriand youth's residence from his father's to his mother's brother's hamlet; but it is of far wider theoretical import than this theme, for Leach deals also with origin myths, incest and exogamy, political hierarchy, local groupings, land-holding, economic obligations, and why the Trobrianders happen to have four clans. It is a little chastening to reflect that such ingenuity as Leach displays is required to give systematic conviction to Malinowski's renowned data and to order the facts of Trobriand life as the people themselves do. This fascinating structural analysis shows how necessary and profitable it is to take native categories seriously, and how essential it is to understand the social structure if we are to grasp what the terms denoting these categories mean. The essay bears the marks of a sociological classic, and alone would justify the launching of a new publication. Its author is to edit and introduce the second number in the series—on caste—and one eagerly awaits this as any vehicle for the ideas of one of the most fertile and penetrating minds in social anthropology.

Rodney Needham

EXPERIMENTAL STUDIES OF PERCEPTION

Readings in Perception

Selected and Edited by Prof. David C. Beardslee and Prof. Michael Wertheimer. (The University Series in Psychology.) Pp. xiii + 751. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1958.) 66*s*.

THIS book is a valuable attempt to represent the present position in the experimental psychology of perception, and to some extent also the steps which have led up to that position, by means of outstanding papers and chapters from important books. The result is an extremely interesting and often rather bewildering collection of fifty-two selections grouped under five main headings.

The authors consider that they have selected studies which represent the core of the experimental psychology of perception, upon which so much current research in the fields of personality, motivation and social psychology is built. They have included a large number of recent investigations, which show the reader clearly what has been and is being done in the study of perception, and will certainly give him a vivid impression of the tremendous interest, complexity and difficulty of the tasks of research. Some of the papers are models of clear thinking, lucid exposition and decisive conclusions. The instructive quality of others lies partly in the evident difficulty of satisfactorily controlling the experimental conditions, and/or drawing conclusions upon which confidence may be placed. Some papers are models of nearly unreadable prose, but in a collection in which the level of specialization of the contributions is unavoidably so varied, this may be inevitable. The editors have also wisely included some papers of classical interest, provided they have not been rendered obsolete by more recent research. These are landmarks for the reader. It is illuminating that in passing from the work of men of outstanding genius to that of ordinary experimenters there is often such a vivid impression of the differences between them. The problem of classification of the papers chosen seems to have been a very difficult one, and anybody reading the book or taking parts of it for discussions, lectures or seminars, would probably have to re-arrange the papers in an order which he felt to give a rational sequence.

The main themes covered by the book are: (1) biological factors in perception (two papers); (2) psychophysical measurement (one paper); (3) perception of objects and events, divided into five sections, (*a*) the stimulus field and its differentiation (four papers), (*b*) perception of organized figures and areas (twelve papers), (*c*) effects of learning and limited experience (four papers), (*d*) perception of successive and changing stimuli (seven papers), (*e*) space perception (eleven papers); (4) imagery and fantasy (three papers); (5) recognition and identification of figures, divided into two sections, (*a*) perception of words as stimuli (five papers) and (*b*) perceptual categorizing (three papers).

In reading the book it is interesting to consider whether the editors might not have done better to re-write the whole mass of material in their own words. At least the length of many papers could have been greatly reduced with advantage. Much boring matter could have been eliminated, and the essential points could have been brought into clear focus. However, in doing this, they might have lost the unique quality which belongs to the thought and writing of many of the gifted authors represented in the collection.

R. W. PICKFORD

EARLY STEAMBOATS

The Birth of the Steamboat

By H. Philip Spratt. Pp. 149 + 11 plates. (London: Charles Griffin and Co., Ltd., 1958.) 28*s*. net.

THIS authoritative little book has clearly been a labour of love on the part of the author and it will be of interest mainly to the specialist rather than to a general reader.

The subject-matter is grouped under the three main headings of "Inventive Aspirations", "Experimental Steamboats" and "Steamboats in Service", and each chapter then deals in chronological order with the various inventors, experimenters or builders who had any effective impact on steamboat development. The book thus tends to be rather episodic, but the author attempts to overcome this by inserting cross-references in the text where necessary. There is a good index, and the list of references is impressive: 390 of them from libraries in Great Britain, the United States, France, Canada, Italy, Germany and Spain.

The material is given factually and without bias. The great names stand out and one cannot help but feel disappointment that the great French pioneer, the Marquis Claude de Jouffroy d'Abbans, was not successful with his fine vessel, *Charles-Philippe*; the ratchet mechanism that he used to drive the paddles proved defective. One of the most likely early vessels was one built by the partners, Fourness and Ashworth, of Yorkshire, having three steam cylinders acting on a three-throw crankshaft driving two paddle wheels. It is described as having undergone "severe tests on behalf of the Prince Regent". Unfortunately, the vessel was soon afterwards mischievously burnt before it had any chance of extended service.

The book clearly brings out the reasons for the failure or success of most of the vessels tried and, as well, it emphasizes that the success attained by that great American steamboat pioneer, Robert Fulton, was considerably due to his willingness to make himself familiar with the work of others in the use of steam and adapt their ideas to his own use. He made no claim to invention but concentrated his attention on well-tried mechanisms and tested hull proportions.

The book closes at 1822 with the development of the first iron-built steamer to put to sea, *Aaron Manby*, and the author has completed a volume which gives the background of the endeavour and the efforts, the triumphs and the failures of those pioneers who made modern ocean commerce possible.

In talking of the size of machinery, reference is often made to a figure for 'nominal horse-power'. It would have added to completeness if a definition of this term had been included.

A. W. JONES

MODERN TAUBERIAN ANALYSIS

Tauberian Theorems

By Prof. H. R. Pitt. (Tata Institute of Fundamental Research Monographs on Mathematics and Physics, No. 2.) Pp. x + 174. (London: Oxford University Press, 1958.) 37*s*. 6*d*. net.

THE integral transform:

$$f(x)=\int k(x,y)\,g(y)\,\mathrm{d}y$$

where k is a given kernel, defines f, in a sense, as an average of g; hence we might expect that while properties of f will follow the type of properties of g, the converse inference will not usually be possible without supplementary conditions. Thus Abel's theorem, that if Σa_n is convergent, lim $\Sigma a_n x^n$ exists as $x\to 1$, has a false converse, which becomes true if supplementary conditions are laid on the a's. Tauber (1897) gave the condition $na_n \to 0$, but this, though sufficient, is not necessary.

The first phase of Tauberian theory began in 1910, when in spite of formidable difficulties, Littlewood showed that a sufficient condition for the Abel converse is that na_n should be bounded; the distinction between tending to zero and being bounded marks a general and characteristic difference between the 'elementary' and the 'deep' theorems in this field. The Hardy–Littlewood partnership then obtained and exploited numerous Tauberian theorems. The second phase dates from about 1923, when Wiener showed that practically all the known Tauberian theorems could be expressed in terms of integral transforms with kernels of the type $k(x-y)$, thus shifting emphasis from results about summation processes for divergent series to a more general theory of transforms. Since then the theory has branched out in several directions, and a comprehensive treatise would be voluminous. But along the main lines laid down by Hardy–Littlewood and Wiener, simplifications and generalizations have been made by many workers, among whom Prof. Pitt has been prominent.

He has now organized this material into a single short volume, the second in the series of monographs on advanced topics sponsored by the Tata Research Institute of Bombay. It is a book for the professional mathematician contemplating work in this field, and a fair degree of sophistication is needed to follow the clear but very concise reasoning. There are chapters on the Hardy–Littlewood and Wiener theorems, and one on theorems developed from Mercer's result (1907), that if σ_n is the mean of $s_1, \ldots, s_n$, and $\alpha > 0$, the convergence of $\alpha s_n + (1-\alpha)\sigma_n$ implies the convergence of s_n; this has the remarkable air of being a Tauberian theorem without a Tauberian condition. Finally, there is a chapter on the prime number theorem; here it appears essential to work with means related to the primes, so that Tauberian theorems are obviously relevant. But Pitt points out that neither the Ikehara-Landau proof, perhaps the simplest, nor the recent Selberg-Erdös proof, certainly the most elementary since it demands no knowledge of Riemann's ζ-function, uses Wiener-type Tauberian theorems, and he offers some pointers towards a study of general Tauberian theorems which are not of Wiener's type. If this prompts some young research worker to investigate the topic, the author and the Tata Institute should be gratified. T. A. A. Broadbent

MAGNETIC AMPLIFIERS

The Theory and Design of Magnetic Amplifiers

By Dr. E. H. Frost-Smith. (Automation and Control Engineering Series.) Pp. xix + 487. (London: Chapman and Hall, Ltd., 1958.) 75*s.* net.

THIS well-written and comprehensive book can be recommended to both students and professional engineers, and many will wish that it had appeared earlier.

The introductory chapter is noteworthy for the emphasis which it puts on mean rectified values of voltages and currents in terms of which transductor characteristics are conveniently described. Two chapters are then devoted to the principal parameters and characteristics, both steady-state and transient, of transductors with idealized core-materials. From this basis the theory of self-excited and auto-excited transductors with practical core-materials and imperfect rectifiers is developed and the influence of reactive loads is discussed.

A short chapter on the theory of control systems is included and a further treatment of the dynamic response of transductors with resistive and reactive loads is discussed in terms of control-system theory. This leads naturally to the need for quick-response transductors in control systems and an admirable chapter is devoted to half-wave, full-wave and three-phase transductors having short-response times.

The three chapters which follow deal with balanced magnetic amplifiers, low-level signal amplification and cascaded amplifiers, and magnetic modulators.

The section on design summarizes the properties of core-materials and their influence on transductor characteristics. A design procedure is developed and is illustrated by three examples, one of which extends to the overall performance of a magnetic-amplifier position-servo. The mixture of units with which engineers still have to deal, despite the adoption of the M.K.S. system for basic equations, is apparent in this chapter.

The final chapter on applications covers a wide field and leaves no doubt as to utility of transductors.

Most chapters have concluding summaries and these, together with the list of references to original papers, make this book a valuable acquisition for engineers entering this field. J. G. Henderson

TREES OF BRITAIN

Trees of Britain

By Dr. Robert Gurney. Pp. 228 + 18 plates. (London: Faber and Faber, Ltd., 1958.) 30*s.* net.

THE late Dr. Robert Gurney had wide biological interests and collected a great deal of information from his own painstaking observations over a period of many years, particularly around Oxford (his home) and in Norfolk. Trees were, perhaps, his primary interest in his later years, and an earlier book of his, "Our Trees and Woodlands" (Medici Society, 1947), will be known to many. The present volume possesses certain special features that are not to be found in the usual books dealing with trees in the British Isles. Most of the books that have appeared hitherto have dealt either with the native trees or with the introduced trees, grown for ornament or for timber. In the present volume Dr. Gurney deals with both these categories, covering all the common trees, wild or cultivated, that are to be found throughout the country. About one hundred different species are dealt with, each receiving separate treatment. The general information accompanying each description includes facts concerning the origin of each species, date of introduction to Britain (where known), general behaviour and growth characteristics. The clear line drawings that accompany each description are a notable feature of the book. They are the work of Dr. Gurney himself, and they usually include a drawing of the seedling, which the author raised from seed which he had himself collected. Another feature of the book is the emphasis that has been placed on buds or bud morphology, and bud development, the features brought to light being illustrated in the drawings. In addition to line drawings there are photographs showing individual trees or groups of trees in various parts of the British Isles. These are all pleasing or exceptional photographs of their kind and may well have been selected for their æsthetic value.

In the section on "Conifers and their Allies", all the species yielding softwoods of importance in Britain or of use in other respects are described. A table giving the dates of introduction of coniferous trees to Britain is of interest. From this it appears European spruce (*Picea abies*) is the earliest introduction (1548), while *Metasequoia glyplostroboides* is the most recent (1948). It is of interest to note that two important conifers, Japanese larch (*Larix leptolepis*: introduced 1861) and western hemlock (*Tsuga heterophylla*: introduced 1863), have not yet been in cultivation for a hundred years in the British Isles.

F. N. Howes

How to Know Western Australian Wildflowers

By William E. Blackall and Dr. Brian J. Grieve. Part 2: A Key to the Flora of the Temperate Regions of Western Australia. Pp. xxxiii + 321–460 + lvii. (Nedlands, W. A.: University of Western Australia Press, 1956.) 30*s*.

SINCE Gaston Bonnier and G. de Layens—with their classic "Flore de la France", published so long ago as 1887—introduced the illustrated-key type of flora, there have been many imitations. The book noticed here is the first example dealing with any part of the flora of Australia and is, in the reviewer's opinion, a good example of this type of flora. Actually the present work is Part 2 of a book first published in 1954, this part containing families 60 to 72 of the original scheme and also the family Goodeniaceae which is of especial interest in Western Australia. Dr. Blackall's original manuscripts have again been worked up by Dr. Grieve and the whole checked against as much fresh and dried material as could be obtained. From examination of the keys forming the flora it is clear that the results of monographic or other specialist work have been fully incorporated.

On the whole the drawings accompanying the different alternatives presented in the keys illustrate well the characters mentioned in the text, though in some cases the small scale makes it difficult to show the special features as clearly as one would have liked. This, however, is a common defect in such illustrated floras. Small sketches of all the species keyed-out help the student to confirm the correctness of his determinations. A complete key to the families in the whole flora is included, while the index to the species gives the authorities for the names and also the distribution according to a standard map provided. There is also a useful glossary. In addition to the many drawings in the key itself, there are five coloured plates which illustrate some of the more striking plants included in this part. Altogether, Dr. Grieve is to be congratulated on the continuation of a useful book. V. S. Summerhayes

The Cherry Kearton Animal Book

By Cherry Kearton. Pp. 168 + 16 plates. (London: Hutchinson and Co. (Publishers), Ltd., 1958.) 12*s*. 6*d*. net.

SOME of the best stories and anecdotes of Cherry Kearton's pet animals have been incorporated into this entertaining volume. In it the reader will meet Simba, the intrepid fox terrier, whose adventures in Africa are a far cry from his acquisition by Cherry Kearton at the Battersea Dogs' Home, and Toto, the intelligent and mischievous chimpanzee who accompanied his owner on some of his African travels. Another section of the book illustrates the wide range of Cherry Kearton's interest in animal life and recounts his friendships with a penguin, an Algerian sand rat and a trapdoor spider. The book closes with some stories of Mary, in her time probably one of the best known chimpanzees in the world, whose accomplishments seem at times to be almost human.

Cherry Kearton's pleasant and easy style carries the reader effortlessly through these stories of his animal friends, and throughout them there runs his understanding that patience and kindness are the only ways to gain the trust and affection of animals. The book is illustrated with photographs of its characters, and in addition there are a few photographs of animals in their natural setting. There is little to criticize: deer do not occur in Africa and three of the photographs have little relation to the text. The book has an obvious appeal to children, and is an admirable introduction for them (and perhaps for their parents) to the writings of Cherry Kearton. J. E. Hill

Nuclear Reactor Metallurgy

By Walter D. Wilkinson and William F. Murphy. With a chapter by Warren J. McGonnagle. Pp. viii + 382. (Princeton, N.J.: D. Van Nostrand Company, Inc.; London: D. Van Nostrand Company, Ltd., 1958.) 42*s*.

THIS book is based on a course of lectures given at the Argonne National Laboratory since 1955. Appropriately, at least half of it deals with uranium, which is treated in detail from the ore to radiation damage in the reactor in a series of chapters. Other chapters deal with plutonium, thorium, ceramics, canning and control rod materials, liquid metals, and radiation damage in engineering materials. A final chapter on non-destructive testing is contributed by Warren J. McGonnagle. In general, the treatment of the chemical and metallurgical engineering topics is much better than that of the physical topics. The important effects of thermal and irradiation strains on the mechanical properties of uranium are overlooked, and the discussion of specific heats and thermal conductivity in Chapter 6 is very weak. Radiation damage in graphite is dismissed in four lines. This latter, as well as the omission of a discussion of magnesium as a canning material, is perhaps understandable since the authors confine themselves mainly to American reactors; but it will disappoint British readers. The chapter on liquid metals is interesting, as are also those on thorium, beryllium, and zirconium, and the book as a whole serves as a useful partial account of the science of reactor materials. A. H. Cottrell

Truth and Denotation

A Study in Semantical Theory. By Prof. R. M. Martin. Pp. xii + 304. (London: Routledge and Kegan Paul, Ltd., 1958.) 42*s*. net.

THIS is likely to be a useful book, both to the specialist and to anybody who is prepared to take some trouble to read and think carefully about formalized languages and their place in the methodology of science. It will go some way to answer the question as to why mathematicians and logicians invent the particular signs and symbols which are now becoming almost common coin. The first chapter deals in general with this theme, whereas the rest of the book is an able and clear discussion of the machinery, including such topics as first-order languages, syntax, non-translational semantics, and the theory of sets and types.

It is well to recollect that it is a feature of non-translational meta-languages that they are not strict translations of the object language. Thus is introduced the relation of 'comprehension'. The importance of this, among other things, is that the classical system of Aristotelean logic is not very satisfactory, when *relations* are involved; but from here, with one semantical primitive, one can build up a species of extended Boolean algebra. It will be interesting to see whether it will stand up to the desire of some applied mathematicians to use these methods for complex electrical networks. Considerable success has already attended efforts to do so with some of the 'classical' Boolean equations. F. I. G. Rawlins

THE ROCKEFELLER INSTITUTE, NEW YORK: A NEW GRADUATE UNIVERSITY

By L. J. F. BRIMBLE

History and Constitution

IN the United States, it was considered that up to 1900 the growth of medical science had not kept pace with the physical sciences, despite the constantly increasing rate at which medical research had been carried on in American universities. Therefore, Mr. John D. Rockefeller accepted the expressed opinion of his adviser, Frederick T. Gates, that "medicine could hardly hope to become a science until it should be endowed, and qualified men be enabled to give themselves to uninterrupted study and investigation, on ample salary, entirely independent of practice". As a result, the Rockefeller Institute for Medical Research was founded in New York during 1901 by Mr. Rockefeller "to conduct, assist and encourage investigations in the sciences and arts of hygiene, medicine and surgery, and allied subjects, in the nature and causes of disease and the methods of its prevention and treatment, and to make knowledge relating to these various subjects available for the protection of the health of the public and the improved treatment of disease and injury . . . to use by any means . . . including research, publication, education, and the establishment and maintenance of charitable and benevolent activities, agencies and institutions appropriate thereto . . .".

The original Board of Directors, comprising William H. Welch (president), T. Mitchell Prudden, L. Emmett Holt, Theobald Smith, Christian A. Herter, Herman M. Biggs and Simon Flexner first set out to study the availability of adequately trained younger men in universities for the furtherance of medical research. The first rented buildings, at 127 East 50th Street, were directed by Simon Flexner, and there investigations in pathology, bacteriology, physiology and biological chemistry were conducted, thus immediately establishing medicine as a science. Later, Mr. Rockefeller purchased the land overlooking East River in York Avenue at 66th Street which now forms the present campus of the Institute. There he had built a laboratory, now known as Founder's Hall (Fig. 1) which was completed in 1906, and this provided space for experimental surgery and experimental biology in addition to the subjects already mentioned.

In 1908, Mr. Rockefeller provided further funds for the establishment of a hospital and isolation pavilion (Fig. 2). This was opened in 1910 with Rufus Cole as director. To this day, only patients of special scientific and medical interest are admitted on the recommendation of a panel of medical men. There they receive exceptional treatment and excellent service and nursing. In return for this they may be looked upon as contributing their diseases for the benefit of medical learning, for no payment is allowed, whether they be rich or poor.

At the same time, a Corporation was set up with increased powers. It included a Board of Trustees as well as the original Board of Directors, the name of the latter having meanwhile been changed to Board of Scientific Directors. The first president of the new Corporation was Frederick T. Gates (adviser to Mr. Rockefeller), and on his death in 1929 he was succeeded by Mr. John D. Rockefeller, jun., who, after twenty-one years service, was followed by his son, Mr. David Rockefeller. As time passed, further generous gifts were made by Mr. John D. Rockefeller and his son (Mr. John D. Rockefeller, jun.).

In 1914, a Department of Animal Pathology was established for the Institute near Princeton University under the directorship of Theobald Smith, who was succeeded in 1930 by Carl TenBroek. In 1931, research in plant pathology was also introduced, so that now the Institute could rightly claim to cover all the main groups of living things. In 1951, the work of the laboratories of animal and plant pathology at Princeton was transferred to the campus in New York.

Simon Flexner retired from the directorship of the Institute in 1935, and he was followed by Herbert S. Gasser, who remained in charge until 1953, when he was succeeded by Thomas M. Rivers. Both Dr. Gasser and Dr. Rivers are now directors emeriti of the Institute, and both still have rooms there.

The year 1953 saw extensive re-organization of the Institute, and Dr. Detlev Wulf Bronk was appointed first president of the Rockefeller Institute of Medical Research. Dr. Bronk is also president of the U.S. National Academy of Sciences, chairman of the National Research Council, and one of America's leading physiologists. He has been professor of physiology in Cornell University and professor of biophysics and director of the Johnson Foundation, University of Pennsylvania. Eventually he became president of the Johns Hopkins University (1948–53) before transferring to the Rockefeller Institute. He is a foreign member of the Royal Society. It has not taken very long to prove that the Institute was indeed fortunate in the election of Dr. Bronk.

In 1953, the Boards of Trustees and of Scientific Directors were merged into a single Board of Trustees which now has fifteen members. They are laymen of distinction in public affairs and men of outstanding scientific achievement, in the ratio of about one to one. These include: Mr. David Rockefeller (chairman), Dr. Detlev Bronk, Prof. R. F. Loeb, Prof. G. H. Whipple, Prof. William J. Robbins, Prof. Philip Bard and Prof. Vincent du Vigneaud.

At present, the staff of the Institute includes twelve members emeriti, all of whom have earned international reputations for their researches in the life sciences; twenty-nine members and professors; seven affiliates; nineteen visiting professors, including such authorities as Lord Adrian of Cambridge (physiology), Prof. T. Dobzhansky of Columbia (zoology), Prof. L. Edelstein of Johns Hopkins (humanistic studies), Prof. Ragnar Granit of Stockholm (neurophysiology), Dr. L. J. Haworth, director of the Brookhaven National Laboratory, Prof. J. G. Kirkwood of Yale (chemistry), [the late] Prof. K. V. Linderstrøm-Lang, Carlsberg Laboratory, Copenhagen (chemistry), Prof. A. M. Monnier of the University of Paris at the Sorbonne (functional physiology), Prof. I. I. Rabi of Columbia (physics), Prof. William J. Robbins,

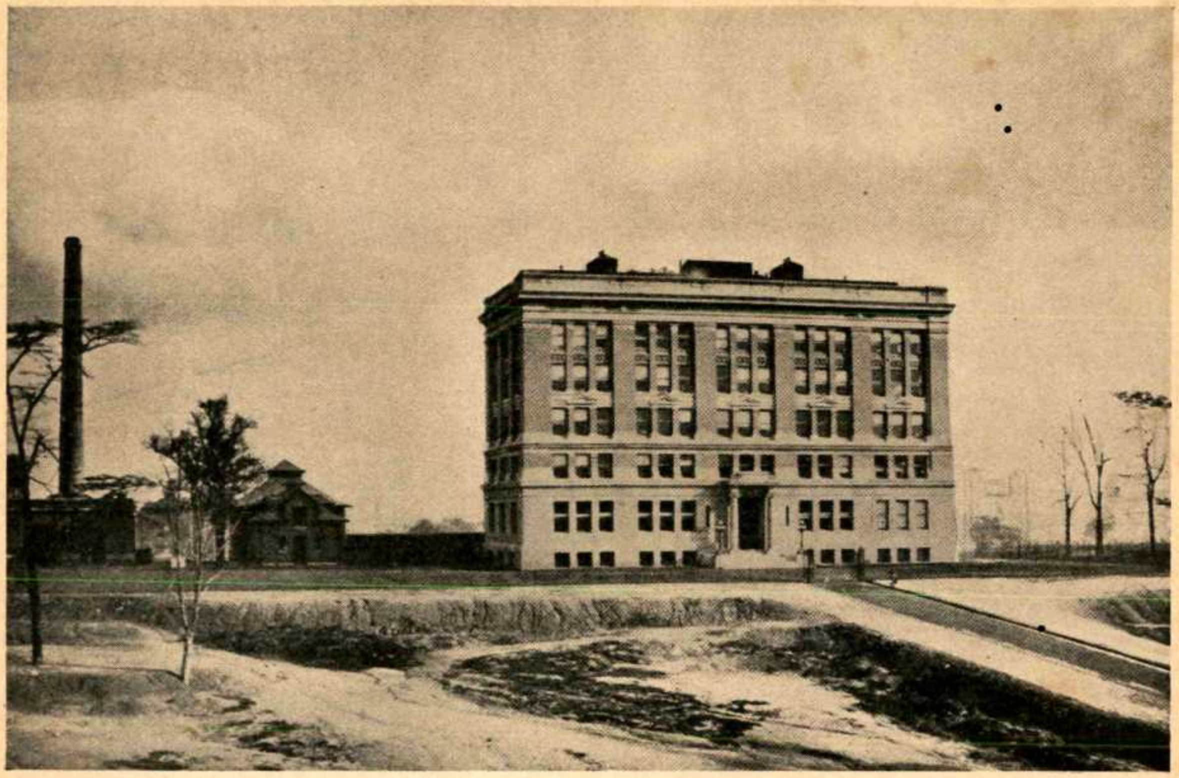

Fig. 1. The Rockefeller Institute for Medical Research as photographed in 1906. Founder's Hall, the only building then in existence

formerly of Columbia (botany), etc.; twenty-four associate professors; thirty-two assistant professors; sixty-two research associates; and forty guest investigators. Prof. Frank Brink is dean of graduate studies, and graduate fellows will this year number 65.

After about fifty years activity, and in order to include graduate education in the natural sciences with special emphasis on the life sciences, the charter of the Institute was amended in 1954 so that it could become part of the University of the State of New York with authority to grant the advanced degrees of doctor of philosophy, doctor of medical sciences, doctor of science (*honoris causa*) and doctor of laws (*honoris causa*). Thus the Institute assumed the status of a graduate university; there are, of course, no undergraduates. It cannot be said, therefore, that the Rockefeller Institute, as a university, is a one-sided affair, for all students have already had those educational and other benefits associated with a full university course before being admitted.

In 1954, the fiftieth anniversary of the opening of the first laboratory, three new buildings were opened, so that then there were Founder's Hall, Welch Hall, Simon Flexner Hall and Theobald Smith Hall, and the Hospital. Since that date, other buildings have been erected and are in use, whereas others are undergoing completion. These are an auditorium, a huge laboratory building, a faculty-visiting scientists social centre, a graduate residential hall, a building for seminars and conferences and a President's House. These buildings and the superb landscaping of the campus (Fig. 3) have been rendered possible by gifts from the estate of Alfred H. Caspary and from Mr. John D. Rockefeller, jun., Mr. David Rockefeller and the United States Public Health Service.

In 1958 the charter of the Institute was amended to change its name from that of Rockefeller Institute for Medical Research to the Rockefeller Institute—a wise decision in view of the comprehensive researches in the life sciences which are now being carried out there.

The current market value of the Institute's endowments is more than 160 million dollars. At present, no more than seventy-five students are to be admitted, at the rate of about twenty each year, to read for the degree of doctor of philosophy or doctor of medical science, so that here we have an aggregate body, a community of scientific scholars, living and working under ideal conditions—a place where they can work, think and dream, away from the sometimes excessive demands made by administration and teaching. The students are few, the faculty (staff) are many. Their creature comforts are catered for in an environment at once functional, beautiful and serene.

The entire organization is of a flexible and personal nature, built around individuals rather than departments, thus allowing the maximum freedom for research and study. The subjects at present being pursued are diverse: they include animal pathology, biochemical genetics, biochemistry, biophysics, biosynthesis, cytology, developmental biology, ecology, general physiology, genetics, history of science, immunology, mathematics, medicine, neurophysiology, parasitology, pathology, physical and organic chemistry, physiology of reproduction and plant pathology.

This academic institution must be unique. It is essential that the graduate students fortunate enough to be accepted be capable of self-directed study. Teaching is mainly done in seminars, tutorial conferences and in faculty research laboratories. The first three months of each initial academic year are devoted to lectures, seminars and discussions in many fields of natural science. Each week a topic in basic science is discussed by one or more members of the staff. Thus, at the outset of his career the student is enabled to develop a broad foundation of competence in many related fields of science and to grasp the connexions of his special field of research with other aspects of science. Thereafter, the educational programme is designed to suit the needs and interests of each individual student. As soon as the student has formulated a significant problem for investigation, he is encouraged to begin research either independently or under the direction of one or more members of the faculty, knowing full well that extraordinary physical facilities for research are at his disposal.

Moreover, in close proximity to the Institute are opportunities for satisfying interests in the theatre, art, literature, music and other branches of science, and fellowship stipends are of a magnitude to permit students to take some advantage of these (see, for example, *Nature* of May 16, p. 1365). Truly, an international centre of research and culture, for, as the supervisor of one of the Halls remarked: "These students and research workers are also men and women". They look not only inside but also outside the Institute for full development and—the main aim of education—complete living.

First Convocation

The first Convocation of the Rockefeller Institute as a graduate university was held during May 21–22. It opened with a luncheon attended by about three hundred guests, including members of the Rockefeller family, some other prominent Americans and distinguished scientific and academic guests.

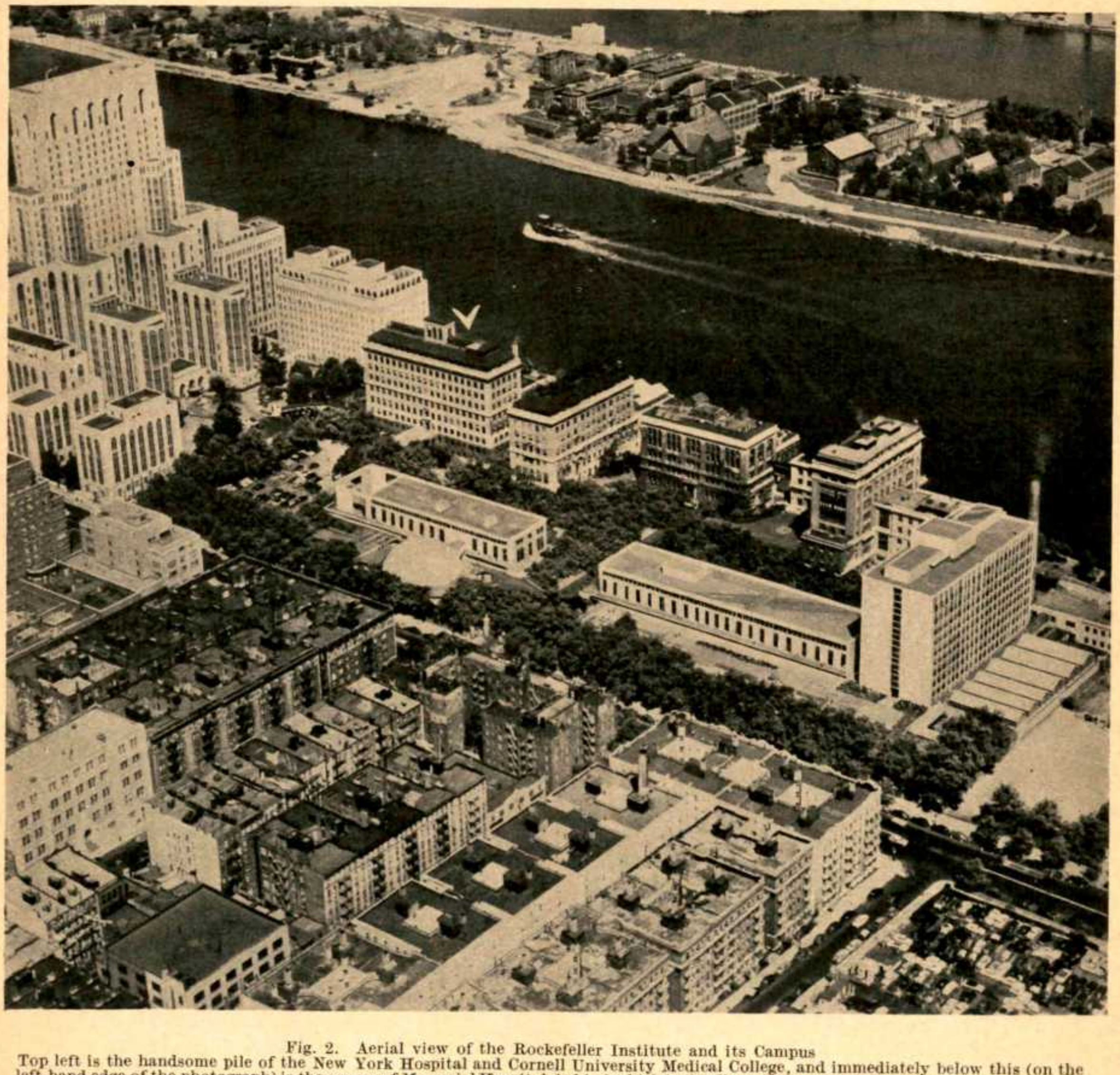

Fig. 2. Aerial view of the Rockefeller Institute and its Campus
Top left is the handsome pile of the New York Hospital and Cornell University Medical College, and immediately below this (on the left-hand edge of the photograph) is the corner of Memorial Hospital, behind which is the Sloan–Kettering Institute for Cancer Research. The arrow indicates Theobald Smith Hall of the Institute, behind which is the President's Residence—a beautiful home built in contemporary American style and commanding a magnificent view of East River. Passing to the right are: Flexner Hall; Founder's Hall (see Fig. 1); behind this on the lower slopes facing the River is Welch Hall; the Hospital. On the extreme right are the new laboratories which are nearing completion. Next to this, and facing York Avenue, is the Graduate Students' Residence Hall. Further to the left are Caspary Hall and Abby Aldrich Rockefeller Hall (both included in one building), in front of which is the dome-shaped Caspary Hall Auditorium

In the afternoon, four commemoration addresses (to be published in later issues of *Nature*) were delivered by: Dr. Detlev Bronk, president of the Institute and of the U.S. National Academy of Sciences; Dr. Douglas M. Knight, president of Lawrence College, one of America's leading undergraduate colleges; Lord Adrian, Master of Trinity College and vice-chancellor of the University of Cambridge; and Dr. Henry A. Moe, secretary-general of the John Simon Guggenheim Memorial Foundation and president of the American Philosophical Society.

A reception and dinner were held in the evening, followed by a concert in the auditorium of Caspary Hall. This concert was given by a section of the New York Philharmonic Orchestra conducted by Carlos Surinach. Apart from one item, the pieces played were by contemporary composers—all American except for one Japanese and one Mexican. Introductory remarks by the conductor and the presence of some of the composers rendered this musical occasion one to be happily remembered, for the presentation was exquisite. Even he without an ear for music or he who usually cannot understand or appreciate the modern musical idiom could not help but be impressed by such a full-blooded and enthusiastic performance.

Dancing followed inside and outside the Abby Aldrich Rockefeller Hall under a full moon.

The proceedings on the following day were initiated by the first graduation of this new university—a completely honorary graduation, for the first so-called 'earned' graduation was to be held a few weeks later. The degree of doctor of laws (*honoris causa*) was conferred on the highest academic officers of six of the oldest universities in Europe and the Americas and on Mr. John D. Rockefeller, jun. With the exception of the last-named, the recipients were presented in order of age of the institution they represented.

Dr. G. G. Forni, rector of the University of Bologna, was presented by Prof. R. Dubos, professor of pathology and microbiology in the Institute. Bologna is the oldest of Europe's universities: by tradition it was founded in 1088, though the names of some teachers in Bologna have survived in parchments dating from 1067. By the year 1200, Bologna had some 10,000 students, most of them from foreign lands. Throughout the centuries, this University has been able to count among its alumni such great names as Dante, Petrarch, Copernicus, Malpighi, Margagni, Spallanzani, Galvani and Marconi.

Dr. T. S. R. Boase, president of Magdalen College and vice-chancellor of the University of Oxford, was presented by Prof. G. W. Corner, historian of the Institute. Oxford is the oldest university of the English-speaking world, dating from the reign of Henry II, when, in 1167, foreign-born scholars were driven from Paris. As pointed out by Prof. Corner: "in the year 1649, three hundred and ten years ago, a handful of scholars, vanguard of the new era in experimental science, founded the Philosophical Club, cradle of the Royal Society, exemplar of our National Academy of Sciences". Oxford has been called the 'home of lost causes'; but this is only another way of saying that she is for ever the home of a cause our world must never lose—the cause of liberty to study, think and teach with untrammelled mind in the free city of the spirit.

Lord Adrian, Master of Trinity College and vice-chancellor of the University of Cambridge, was presented by Prof. Peyton Rous, professor emeritus of pathology and microbiology in the Institute. Cambridge also dates back to the twelfth century, and was granted its charter during the reign of Elizabeth I. Oxford and Cambridge "have gone forward side by side throughout almost seven hundred years and have been competitors along most of the way, however impersonal their scholars. Together they emerged from Scholasticism, changed with the Reformation, weathered the Puritan Revolution, the Georgian Era; and yet despite all vicissitudes neither has gained superiority over the other when viewed in the sharp light of the present. Where else does such a state of affairs obtain amongst old universities? Can it be that the love of the English people for contests under fair terms has extended far beyond boat races that almost subconsciously, by giving and taking in a myriad ways, they have maintained the great rival universities in balanced power?"

Dr. J. L. Barandiaran, rector of the University of San Marcos, Lima, Peru, was presented by Prof. R. E. Shope, professor of animal pathology in the Institute. The University of San Marcos was founded in 1551 by royal decree issued by Charles V of Spain. Since that time, it has developed a distinguished record as a centre of intellectual leadership.

Dr. Nabor Carrillo, president of the National University of Mexico, was presented by Prof. Paul A. Weiss, professor of developmental biology in the Institute. This University was also founded in 1551 by Charles V of Spain. It now has a large number of students and teachers working on what must be one of the most beautiful and impressive campuses in the world.

Dr. N. M. Pusey, president of Harvard University, was presented by Prof. A. E. Mirsky, professor of general physiology in the Institute. Harvard, the oldest college in the United States, was founded in 1636 with a gift of £400 from the General Court of the Massachusetts Bay Colony. In the same year, John Harvard, of Emmanuel College, Cambridge, and a Puritan immigrant, bequeathed to the seminary £780 and 260 books; the College was then re-organized, and in 1639 was named Harvard College. Such alumni as Lowell, Longfellow, Agassiz and Emerson have left their stamp on that University; and such presidents as C. W. Eliot, A. L. Lowell and J. B. Conant influenced the entire course of American education.

Owing to his indisposition, the degree of doctor of laws (*honoris causa*) was conferred on Mr. John D. Rockefeller *in absentia*. His son, Mr. David Rockefeller, received the insignia of the degree, after a moving citation by Dr. Detlev Bronk. John D. Rockefeller was born on January 29, 1874, and in 1901 he married Miss Abby Greene Aldrich. They had one daughter and five sons—John D. 3rd, Nelson A. (now governor of New York), Laurance S., Winthrop and David (chairman of the Board of Trustees of the Institute). His life has been devoted to the philanthropic and civic activities of the Rockefeller family, particularly those designed to advance human welfare and those furthering international, inter-faith and inter-racial concepts. He has been active in the organization, administration and policy development of these activities and has made many of them financially possible. He was associated with his father in the creation and development of the Rockefeller Institute for Medical Research in 1901, the General Education Board in 1902, the

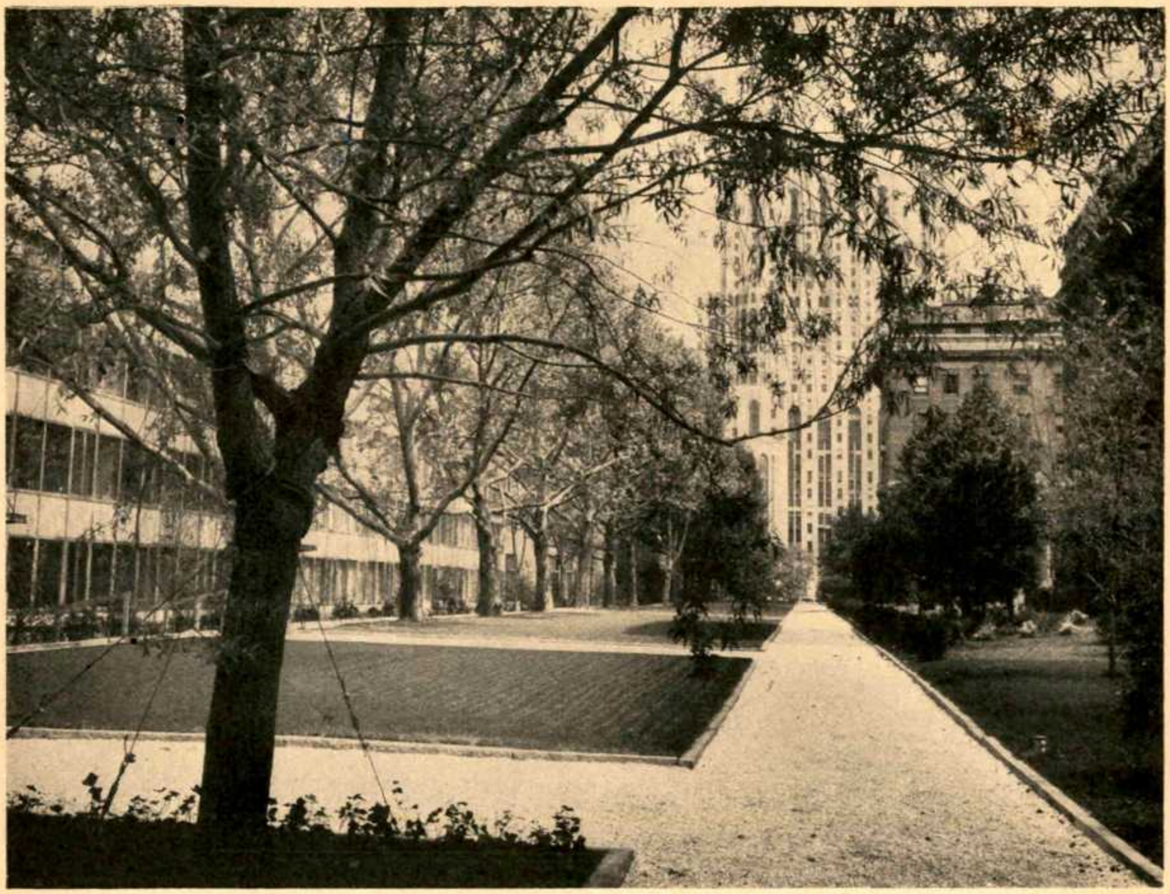

Fig. 3. View of the new campus area of the Rockefeller Institute, looking toward New York Hospital. On the left is the Graduate Students' Residence Hall and, on the right, one of the Institute's older laboratory buildings (Flexner Hall)

Rockefeller Foundation in 1913 and the Laura Spelman Rockefeller Memorial in 1918. The last two were merged in 1928. Thus father and son have, as Dr. Bronk said, "been unequalled in their sympathetic understanding, their selfless service, and the scope of their unrestricted, generous gifts in support of scholars and their corporate institutions".

Dedication of New Buildings and Campus

Five new buildings and the North and South Campus were dedicated during the afternoon of May 22. Of necessity in New York, though the buildings are large and spacious, the total area of the campus is comparatively small. This has much to recommend it ; for the tendency among some modern universities is to spread themselves over huge areas, thus rendering intercommunication inconvenient if not exhausting.

Caspary Hall contains an auditorium to hold five hundred, numerous seminar and conference rooms, and rooms for the Board of Trustees and senior administrative officers concerned with the educational activities of the Institute. The auditorium is dome-shaped, and its furnishings are of striking beauty. The acoustics are excellent.

Abby Aldrich Rockefeller Hall contains social halls, refectory, library, meeting rooms and private dining rooms for the friendly association of members of the faculty and their families. It also provides living quarters for visiting scientists so that this building may become an international scientific centre for meetings and the exchange of ideas. The air-conditioned residential suites leave nothing to be desired, and the library, refectory and lounges are adorned by some impressive, though controversial, examples of modern American art.

The President's House likewise fosters the development of the Institute as a centre of scientists in a great international city.

The Students' Residence Hall is designed to meet the needs of the most fastidious.

The South Laboratory (Fig. 2) is a huge building which will soon be offering comprehensive facilities for research in many fields.

The campus is charmingly landscaped (Fig. 3).

Of the older buildings, Founder's Hall, Flexner Hall and Theobald Smith Hall are devoted primarily to the housing of 109,000 sq. ft. of laboratories, most of which have been reconstructed and re-equipped within the past ten years. The Hospital, of fifty-six beds, serves as a laboratory for the study of the physiology of man and certain of the diseases which afflict him. Greenhouses provide approximately 10,000 sq. ft. of facilities for botanical research.

Welch Hall contains a library of more than 40,000 volumes, including an unusually fine collection of scientific periodicals. In this building there are also a large faculty dining hall, another for the women of the administrative, secretarial and technical staffs, and social rooms for both groups.

Other buildings comprising the Institute are the Jacques Loeb Laboratories in the Marine Biological Laboratory at Woods Hole, Mass., for those wishing to study marine organisms. Special facilities are also available in the research laboratories of the New York Botanical Garden for those members of the faculty who desire to use the extensive resources there.

Because of increasing dependence of modern scientific research on adequate technical facilities, many supporting services are maintained in order to facilitate and make more effective the work of the Institute. For example, the Animal House contains 40,000 sq. ft. of quarters for animals ranging in size from mice to horses. There are well-equipped shops for the construction of instruments and electronic equipment; whereas shops for machine work and cabinet work make possible the construction and maintenance of all laboratory equipment. Central facilities for electron microscopy, spectroscopic determinations, microanalyses, X-ray studies, photographic work and media preparation are among the many aids maintained for the general use of the various laboratories.

Publications

The Rockefeller Institute Press was established in 1958 and now publishes *The Journal of Experimental Medicine*, *The Journal of General Physiology* and *The Journal of Biophysical and Biochemical Cytology*. Reprints of recent publications are issued periodically as volumes of *Studies*. Events of general interest are published in *The Rockefeller Institute Quarterly*. Monographs and scientific texts are to be published by the Rockefeller Institute Press in association with Oxford University Press.

The celebrations of the first Convocation of the Rockefeller Institute were rounded off by a pleasant garden party in the grounds of the President's House.

In announcing his resignation from the presidency of the Board of Trustees of the Rockefeller Institute in 1950, Mr. John D. Rockefeller, jun., said he had always regarded "this enterprise as the most significant and the most permanent of any that my father established". It is certainly true that the world of scholarship, and especially of science and medicine, owes a great debt of gratitude to the Rockefeller family: particularly through the Rockefeller Institute is the world indebted to John D. Rockefeller, his son John D. Rockefeller, jun., and his son David Rockefeller.

To Dr. Detlev Bronk the world of science and learning will tender their congratulations and express deep admiration for his almost superhuman efforts to further the development and advancement of the Rockefeller Institute and especially for the foundation of this new graduate university.

EVOLUTIONARY SYSTEMS—ANIMAL AND HUMAN*

By Prof. C. H. WADDINGTON, C.B.E., F.R.S.
Institute of Animal Genetics, Edinburgh, 9

THE major advance in the theory of biological evolution since Darwin's day has been the rise of Mendelian genetics. It is scarcely an exaggeration to say that when Darwin wrote biology possessed no theory of inheritance. Since then, the existence of more or less discrete hereditary factors has been discovered, their position in the cell ascertained to be on the chromosomes in the nucleus, and the behaviour of these chromosomes analysed in great detail both in normal and in various more or less unusual conditions.

The whole of this complex of phenomena which are concerned with the manner in which hereditary determinants are passed on from one generation to the next may be referred to as the 'genetic system'. From the point of view of evolutionary theory three main points have emerged concerning it. The first is that the existence of discrete hereditary determinants safeguards variation against being lost if dissimilar animals cross-breed, as Darwin feared it might[1]. Indeed the fact that during the greater part of the life-cycle of most animals and plants the hereditary factors are present in the diploid condition implies that most organisms carry within them much greater potentialities for variation in their offspring than would appear at first sight. The second point, which is one that we owe primarily to the insight of Darlington[2], is that the genetic system itself can be regarded not only as an agent but also as a subject of evolutionary change, which is to say that the genetic system itself evolves. This I shall return to later.

The third point concerns the origin of new variation. It is essential to any theory of evolution that there must be some mechanism by which new variation is brought into being. Darwin was driven to speculate as to what this mechanism might be. In the absence of any understanding of how hereditary qualities are transmitted, he made no pretence that he had found a solution fully satisfactory to himself, although he was somewhat tempted by the theory, usually associated with the name of Lamarck, that characters acquired by organisms in the course of their lifetime might be transmitted to their offspring. Later experimental investigations have shown that in general this is not so.

Our knowledge of the genetic system, which is very extensive and detailed, forces us to the conclusion that the origin of new hereditary variation is to be found only in alterations and rearrangements of the atomic groupings out of which the hereditary factors of the chromosomes are composed. These alterations follow rules of stability which are still entirely unknown to us, but which must be properties of the hereditary molecules themselves and have little or no relation to the precipitating events by which the alterations were stimulated. One of the most firmly based doctrines of modern genetics is that mutation is a random process. I do not wish to challenge this, but I shall suggest later that some care is necessary in interpreting the word random.

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* Substance of the Woodhull Lecture delivered at the Royal Institution on February 27.

In present-day biology, evolution is envisaged as resulting from the interaction between, on one hand, the genetic system characterized by random mutation, and on the other, natural selection. The evolutionary pressures exerted by these two factors are exhibited as being quite external to the nature of the organisms involved. The essential evolutionary pressure exerted by the genetic system is that of mutation, and mutation, it is explained, is a random process. Any explanation which might be offered for the nature of the mutational changes would have to be found, it is asserted, in the chemical composition of the genes and not in the nature of the complete biological organism in which these genes are carried. Mutation thus appears as essentially an external force to which the organism passively submits. Again, natural selective pressures are usually thought of as arising simply from the external environment. When the climate changes, a new predator appears, or industrial fumes blacken the tree trunks on which the animal lives, the populations of organisms concerned cannot, it is usually implied, do anything but submit to these pressures and wait until the equally uncontrollable process of mutation throws up a new hereditary variant which enables them to meet the environment's challenge more successfully.

The time seems to have come when we need to take into account two further aspects of the evolutionary mechanism[3]. In the first place, natural selective pressures impinge not on the hereditary factors themselves, but on the organisms as they develop from fertilized eggs to reproductive adults. We need to bring into the picture not only the genetic system by which hereditary information is passed on from one generation to the next, but also the 'epigenetic system' by which the information contained in the fertilized egg is expanded into the functioning structure of the reproducing individual. Each organism during its lifetime will respond in some manner to the environmental stresses to which it is submitted, and in a population there is almost certain to be some genetic variation in the intensity and character of these responses. Natural selection will favour those individuals in which the responses are of most adaptive value.

Two consequences can be expected to follow, and have in fact been demonstrated experimentally. In the first place, natural selection will build up genotypes which set going developmental mechanisms which easily respond to environmental stresses by the production of a well-organized modification which is of adaptive value. It will, as it were, build into the genotype a gun which is not only set on a hair trigger but which is aimed to hit the target when it goes off. In so far as such a developmental response becomes precisely delimited and easily initiated, it becomes the more likely to be produced by unspecified changes in the chemical nature of the hereditary substance. Mutations, which we can think of as random when we are considering the nucleo-proteins of the chromosomes, will have effects on the phenotype of the organisms which are not necessarily random, but which will be modified by the types of instability which have been built into the epigenetic mechanisms by selection for response to environmental stresses.

Since this is an unfamiliar point of view it may be as well to illustrate it by actual example[4]. If eggs of *Drosophila* are submitted to ether vapour shortly after laying, a proportion of them tend to have their development modified so that they produce a very peculiar phenotype, known as bithorax, in which the third segment of the thorax of the animal is transformed from its normal small and obscure structure into a duplicate of the large second thoracic segment. We can treat the response as though it were favoured by selection, and in each generation breed from those individuals in the population which respond to the stress in this way. When this was done with a population taken from a normal wild-type stock, it became apparent that there was some genetic variation of the capacity to respond in this manner. If selection favoured the response, the frequency with which it occurred increased from generation to generation, until after some time it became practically universal when the selected stock was submitted to the ether. After some time a new gene mutation occurred; this was a sex-linked factor which had not been present in the original stock. Its effect is that females homozygous for it lay eggs which tend to develop the bithorax phenotype. This is particularly striking when the factor is present in the selected stock, in which, as it were, the bithorax modification has been set on a hair trigger. If the factor is transferred into an unselected wild-type stock, the tendency to produce bithoraxes is very much reduced. We have here an example in which selection has built up a genotype which exhibits a particular type of developmental instability. A gene mutation has occurred which in the normal *Drosophila* would have only a very slight tendency to produce this phenotype, but which does so with considerable frequency in the selected stock. Thus, if one merely refers to such a gene mutation as 'random', one does not say by any means everything of interest which can be told about it.

The other main evolutionary effect of the epigenetic system depends on the fact that the development of organisms is usually to some extent canalized, in the sense that even though it may become somewhat modified in response to an environmental stress, it also exhibits a tendency to reach its normal end-result in spite of disturbing circumstances If a strain of animals is selected over many generations for its capacity to respond in a particular way to a certain stress, a set of genotypes will be built up in which this response is easily exhibited when the environmental stress is applied, but the developmental resistance to change may be sufficient to ensure that some of it is still retained even if the stress is removed. If that happens, we should have a system which exactly mimics the inheritance of an acquired character, but one which depends not on the direct induction of a hereditary variation, in the manner suggested by Lamarck, but on selection operating on the genetical structure of the population.

Again, there is a practical chapter and verse for such a suggestion in the experiments with the bithorax modification. After rather more than 20 generations of selection for ease of response to ether vapour, the strain had reached a condition in which a high proportion of bithorax individuals appeared even when the ether treatment was not given. This is the process which I have spoken of as the 'genetic assimilation' of an acquired character.

To obtain a complete picture of the evolutionary system, we need to take into account one further set of factors. These may be spoken of as the exploitive system. Animals—the following considerations do not apply so directly to plants—are usually surrounded by a much wider range of environmental conditions than they are willing to inhabit. They live in a highly heterogeneous 'ambiance', from which

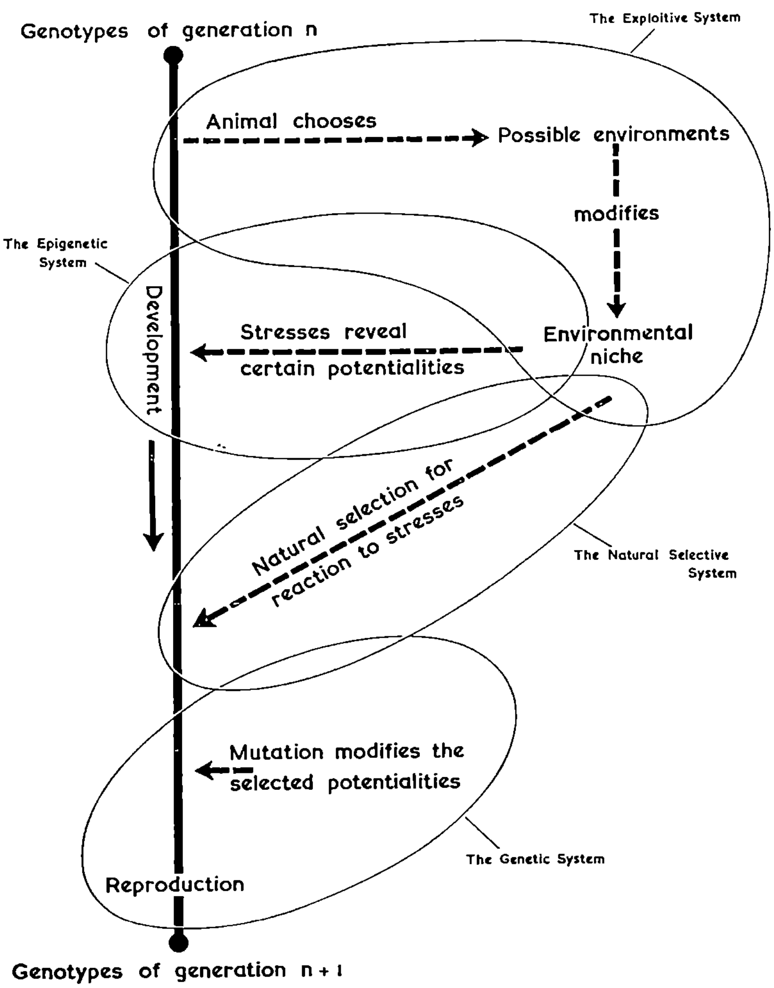
Genotypes of generation n
The Exploitive System
Animal chooses
Possible environments
modifies
Environmental niche
The Epigenetic System
Development
Stresses reveal certain potentialities
Natural selection for reaction to stresses
The Natural Selective System
Mutation modifies the selected potentialities
The Genetic System
Reproduction
Genotypes of generation n + 1

Fig. 1. The logical structure of the biological evolutionary system

they themselves select the particular habitat in which their life will be passed. Thus the animal by its behaviour contributes in a most important way to determining the nature and intensity of the selective pressures which will be exerted on it. Natural selection is very far from being as external a force as the conventional picture might lead one at first sight to believe.

The problems which arise in this field have as yet been rather little studied, even in the biological field, where the relations are likely to be relatively simple. This area of study is, however, likely to be of particular importance for eugenics, since human behaviour is incomparably more elaborate than that of the majority of animals, and in particular the behaviour associated with choice and the seeking of particular goals is much more fully developed.

Biological evolution, then, is carried out by a mechanism which involves four major factors: a genetic system, an epigenetic system, an exploitive system, and a system of natural selective pressures (Fig. 1). All these factors undoubtedly persist in man, but, just as the genetic system is itself subject to evolution, so in broader terms we may say that this whole four-component evolutionary system, of which the genetic system is only a part, itself evolves. The human situation is characterized by an enormously important step in the evolution of the evolutionary mechanism. Indeed, it might be not unreasonable to define humanity by this fact. In man, the processes of teaching by the older members of the population, and learning by the younger ones, have been carried to an incomparably higher pitch than is found in any of the prehuman forms of life, where they play only a relatively minor part, for example, in the determination of bird song, and a few other examples. In man, they have developed not only to highly effective person-to-person learning, as in apprenticeship, but, by the invention of writing and other more recent devices, to an extremely elaborate system by which the whole conceptual understanding of the past is made available to present recruits to human society. We have here what in effect amounts to a new mode of hereditary transmission. It may be referred to as the cultural or 'socio-genetic' system.

Within the past few millennia, the human race has acquired capacities which, in the non-human world, could only have been obtained as the results of evolution. To give a banal example, one may mention the ability to fly. Man has certainly not achieved this capacity by waiting for genes to turn up which have transformed his fore-limbs into wings. In fact there is no evidence that changes in the pool of genes available to the human race had any specific effect on the development of the human conquest of the air. This does not mean, of course, that the genes were irrelevant. Human inventiveness and skill, just like any character of any organism, are produced by the interaction of genes with one another and with the environment during development. But so far as one can tell, all the genes necessary to produce men capable of inventing methods of flying had been present in the human population for many generations. What the development of flight was waiting for was not some change in the genetic system, but some change in the cultural system.

When one attempts to consider the problem of human evolution, the type of phenomena which should rise to one's mind are all the most crucial changes which have occurred between, say, the late Stone Age and the present. It is not in any important sense the slight changes in bodily structure which differentiate us from Cromagnon man which make the greatest impression. Human evolution has been in the first place a cultural evolution.

It is important not to overlook this first impression of what human evolution is all about. It is clear that for an understanding of how the human race has come into the possession of those characteristics which we now think most valuable in human life, a theory is needed which is primarily one of cultural evolution.

It seems probable that in the cultural evolutionary system there are parallels for many of the factors operative in the biological system. For example, parallel to the process of gene mutation there is the arising of new ideas capable of cultural transmission; and there are undoubtedly processes, fulfilling a function similar to that of natural selection, which determine whether newly arisen ideas will in fact be perpetuated in future generations or not. How far is the arising of culturally novel ideas a process which can be characterized as random, even in the restricted sense in which we have seen this term should be used in the biological sphere ? What is it that determines the intensity of the natural selective pressure for or against the preservation of new ideas ? Again, items capable of cultural transmission such as ideas, techniques or skills do not occur in isolation but are found in co-ordinated groups. Can we find here some parallel to the genetic phenomena of linkage and recombination ? The cultural exploitive system, the system of choosing and modifying the environment, is also obviously very highly developed. Again, cultures reacting to external stresses may become particularly liable to modification in certain directions, exhibiting phenomena similar to those we have attributed to the epigenetic system. All these parallels, however, remain as yet very incompletely worked out. It would probably be profitable to pursue them[6].

Although it would seem prudent, when faced by a phenomenon of human evolution, first to consider by what cultural means it has been brought about, it is also very necessary to inquire into the biological or genetical phenomena associated with it. This is, however, exceedingly difficult. Suppose a marked change takes place in the gene pool of the human population; under what circumstances should we expect this to have an important influence on the essential cultural achievements of the group concerned ? It is extraordinarily difficult to find any factual evidence, since most examples of marked changes in the gene pool of a population involve the immigration or emigration of individuals who carry with them not only their transmissible genes but also their transmissible culture. For example, one may postulate, as Darlington[5] has done, that the emigrants from Ireland in the middle of the past century carried out of the population many genes for various types of socially effective behaviour, leaving the home population impoverished. But in practice the existence of these genes is only hypothetical, and even if they did exist the emigrants also undoubtedly carried with them culturally transmitted tendencies to vigorous behaviour.

There are a few cases, however—for example, when Jewish populations have immigrated into or out of a country, with whose population they have not engaged in extensive cross-breeding, but on whose life they have exerted a considerable influence—in which one may deduce that this influence has been primarily a cultural rather than a genetic one. Even if we were to make the unsafe assumption that it is their genes which endow the Jewish people or the Chinese with great ability in trade, the effect which a small number of Jews or Chinese may have on the economic existence of the people surrounding them can only be the result of cultural rather than genetic transmission. Again, the rapidity, in terms of numbers of generations, with which many steps of evolution take place (such as, say, the formation of the characteristic United States culture out of an extraordinarily mixed European immigrant population) is scarcely compatible with the operations of the genetic evolutionary mechanism and, it would seem, must in the main be attributed to the actions of the human cultural evolutionary system.

When we can discern cultural differences between two human groups, does the main responsibility of these lie with the system of cultural transmission or with that of genetic transmission ? Again, from an *a priori* point of view one must expect differences in both systems to be involved, and it is exceedingly difficult to assess the relative importance of the two contributing factors. It is quite clear that races such as the West Africans, the Maoris and the Chinese, differ genetically from Europeans. Some of these genetic differences are obviously expressed in skin colour; there must surely be others, more difficult to detect. But is there any reason, for example, to suppose that it is the differences in the gene pool between the Chinese and the European populations which have caused the one to develop a social system based on such relatively unindividualistic systems as Confucianism and Buddhism and the other a civilization inspired by such a different system of thought and feeling as Christianity ? I see no *a priori* reason to suppose anything of the kind; nor is there sufficient factual evidence to establish such a conclusion.

Again, one can find examples, particularly in quite recent times, in which human populations have undergone important changes in periods of time which seem much too short to allow of noteworthy alterations in their genetic endowment. The change in West Africa from the conditions described a century ago, to the present highly sophisticated and technologically competent modern societies, can only have been accompanied by exceedingly small, if any, changes in the general gene pool. One of the most striking of such changes, and one of the very few that has been carefully studied by a highly trained specialist, is that of the Manus people of the Admiralty Islands in the Pacific, studied by Margaret Mead[7]. This transformation from a palæolithic to at least the beginnings of a modern society has taken place within a lifetime; that is to say, it has involved *no* genetic alteration. It is a most remarkable example of how powerful the cultural evolutionary system may be.

These examples suggest, in my opinion, that in producing the changes of the kind which we consider of major importance in the evolution of mankind, the cultural system of transmission usually contributes incomparably more than the genetical. Even when we can be certain that genetical changes have occurred, as, for example, in the comparison between Africans and Europeans, there are only one or two examples in which these changes can be shown to have any practical importance.

The genetic system of a population, as Lerner[8], in particular, has pointed out, shows a considerable power of resistance to factors such as natural or artificial selection which attempt to alter it. I have argued that the epigenetic system shows similar characteristics of unresponsiveness[3]. One might expect, and I think the evidence suggests, that cultural systems also have some tendency to stability. This is probably correlated to some extent with their size. The fantastically rapid transformation of Manus society occurred in a minute population of only a few thousands; one could scarcely expect the fifty millions of Nigeria or the five hundred millions of China to alter as rapidly. One cannot, therefore, always expect the processes of change mediated by the cultural evolutionary system to occur in a shorter time than those which might be carried out by the genetic system. It is only in favourable cases that the critical evidence emerges which shows that steps in human evolution can occur at a rate much faster than the genetic mechanisms could bring about. Cultural phenomena which involve stability over long periods need not necessarily, on *a priori* grounds, be attributed to the genetical system; there is no reason to doubt that cultural transmission may operate over many generations. Such questions will only be answerable when we find further methods of gathering empirical data which will enable us to distinguish the contributions of the two information-transmitting systems in each particular case.

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[6] Waddington, C. H., "The Human Evolutionary System". Proc. Conference on Darwin and Sociology, Edinburgh, April, 1959 (in the press).

[7] Mead, Margaret, "New Lives for Old" (Gollancz, London, 1956).

[8] Lerner, I. M., "Genetic Homeostasis" (Oliver and Boyd, Edinburgh, 1954).

OBITUARIES

Sir Stanley Angwin, K.C.M.G., K.B.E., D.S.O., M.C.

The death on April 21 at the age of seventy-five of Sir Stanley Angwin brings to a close a remarkable military and engineering career. Educated at Queen Mary College, he received his practical training with Messrs. Yarrow and Co., the shipbuilders. In 1906, at the age of twenty-three, he entered the Engineering Department of the Post Office, a step which took him in the course of fifty years to the highest engineering and administrative positions in the telecommunications field; he became engineer-in-chief of the Post Office in 1939, chairman of Cable and Wireless in 1947 and finally chairman of the Commonwealth Telecommunications Board from 1951 until 1956.

It was provident that Angwin was engineer-in-chief during the Second World War, for the part played by telecommunications was vital and demanded extreme co-operation with the Fighting Services. Angwin had a foot in both the Civil and Services' camps, for he had been associated with the Army Signals since the inauguration of the Territorial Army. His Unit, which he raised as the Lowland Division Telegraph Company, was mobilized in 1914 to form the 52nd Divisional Signal Company and served throughout the First World War in Gallipoli, Egypt, Palestine and France. He was awarded the D.S.O. and M.C., and those who knew his scant personal regard for air raids in 1940 can readily imagine the value and influence of his imperturbable personality as a young commander in the earlier War. His association with Army Signals continued between the Wars, first in command of the 44th Home Counties Divisional Signals and finally as deputy chief signal officer for the Supplementary Reserve.

With this background, Angwin was in an excellent and accepted position to assess and direct the provision of the many long-distance circuits and installations required for the defence of the United Kingdom. The demands for Post Office services were overwhelming, and sometimes competing, particularly for air defence, and later for the U.S. Armed Forces, and the preparations for *D* Day. All this in the face of bomb damage, and incessant repairs, provided a formidable task of direction, while at the same time Angwin fostered the release of technical staff to the Forces for the build-up of the signal staffs and units overseas where their professional knowledge was indispensable.

Between the Wars Angwin's work had been associated with the development of the Post Office and Commonwealth radio services. On his return from the First World War he was appointed to the wireless section of the Engineer-in-Chief's office. There he found, in an era of development, just those opportunities needed to match his many talents. On the technical side he found scope for applying his knowledge and experience in the design and construction of high-power radio stations at Cairo, Leafield and Rugby; and was closely connected with the establishment in 1927 of the first trans-Atlantic telephone service and in the subsequent development of short-wave radio telephone services to all parts of the world.

Angwin's ability in negotiation was equally outstanding. This frequently led to his appointment as chairman of committees, particularly those dealing with controversial matters, at many international telecommunication conferences.

He was chairman of the Radio Research Board during 1947–52. In 1945 he accompanied Lord Reith on a mission to the members of the Commonwealth to discuss changes in Commonwealth communications, leading to the nationalization of Cable and Wireless, Ltd., and to the setting up of the Commonwealth Telecommunications Board.

On retirement from the Post Office, Angwin became in January 1947 the first chairman of Cable and Wireless, Ltd., in its new role, and in April 1951, at the invitation of the partner Governments, followed Lord Reith as chairman of the Commonwealth Telecommunications Board. In 1950, as chief technical adviser to the Board, he had presided over a meeting of technical and traffic experts from all parts of the Commonwealth, which was the first Commonwealth gathering of its kind. He was chairman of the Board for five years, filling this office with his usual distinction and doing much to further Commonwealth co-operation in all spheres of telecommunications. In 1954 he headed a delegation of the Board to Australia and New Zealand. In 1955 he presided over a second successful technical and traffic conference in London, but in 1956, owing to ill-health, he felt obliged to retire.

As engineer-in-chief of the Post Office, Angwin was knighted in 1941 and made K.B.E. in 1945 for his war services. For his services to international telecommunications he was made K.C.M.G. in 1957. He was president of the Institution of Electrical Engineers during 1943–44, Faraday Medallist in 1953 and made an honorary member in 1956. He became a Fellow of Queen Mary College, London, in 1946 and received an honorary degree of doctor of science from the University of London in 1953.

Lady Angwin was an ideal support to him throughout his career. With their family they made their home in Welwyn Garden City, where his charming house and garden must have been a welcome haven in the midst of his exacting duties.

His friends will remember his quiet and seemingly casual manner, his kindly disposition and yet the confidence he could inspire and the force of his leadership. GORDON RADLEY

Mr. L. E. Harris

MR. LAWRENCE ERNEST HARRIS, a leading authority on fen drainage, died on April 5 at Cambridge, aged sixty-six. The Newcomen Society for the Study of the History of Engineering and Technology has suffered a very severe loss by his unexpected death during his second year as president.

After leaving Mercers School, London, Harris studied at the City and Guilds Engineering College, South Kensington, during 1910–12 and won a Mitchell scholarship. He obtained his practical training with C. Isler and Co., London, artesian well engineers. During the First World War he served in the Royal Fusiliers and the Machine Gun Corps and, as a lieutenant, was invalided out due to war wounds. Having taken a refresher course at King's College, London, Harris joined Sulzer Bros., Ltd., as an estimating engineer in their London office. After three months at their Winterthur Works, he went to India in 1923 as the firm's manager, and for thirteen years was responsible for the sale and installation of many Sulzer steam and diesel engines, pumps and electrical machines in pumping and power stations. Returning to England, he was appointed district manager and engineer for the Sulzer organization in the Fen area in 1937, specializing in fen drainage and pumping machinery. He also installed Sulzer pumps for the Somerset River Board's drainage schemes. He lived in Leeds until 1947, and then in Histon, Cambridge, holding the same appointment until his death.

Harris was intensely interested in the history of his subject, and his authoritative book, "Vermuyden and the Fens", was published in 1953. He wrote the chapter, "Land Drainage and Reclamation" in Vol. 3 of "A History of Technology", published in 1957, and contributed to the Newcomen Society "Sir Cornelis Vermuyden, an Evaluation and an Appreciation" and "Some Factors in the Early Development of the Centrifugal Pump, 1689–1851". In his presidential address, "A Neglected Genius of Seventeenth Century Technology", he paid honour to the inventor, Cornelius Drebbel (1572–1633), of Alkmaar. One of Harris's last interests was to ensure that the beam engine and scoop-wheel installed in 1831 at Stretham, near Ely, by the Butterley Company, should be permanently preserved, as it is the last surviving example of the introduction of steam power for fen drainage. The formation of the Stretham Engine Preservation Trust in 1958 was due to him; he was elected the first chairman of the Trustees and wrote the appeal this year for an endowment fund. His many friends hope the appeal will succeed in its object and that it will be a permanent tribute to his memory. He is survived by his widow, Mrs. Kathleen Harris, and his two sons, Michael and John, both engineers. A. STOWERS

NEWS and VIEWS

Special Assistant for Science and Technology to the U.S. President: Prof. G. B. Kistiakowsky

PROF. GEORGE B. KISTIAKOWSKY, a distinguished physical chemist, who succeeds Dr. James R. Killian (*Nature*, 181, 384; 1957) as special assistant for science and technology to the President of the United States, spent four years at Princeton University after receiving the Dr.Phil. in Berlin in 1925. He went to Harvard University in 1930, progressing quickly to a professorship in 1937, which he has held ever since. Following early researches on the ultraviolet spectra of polyatomic molecules, and on thermodynamics, after the Second World War he applied shock and detonation waves to the study of chemical problems, determining the heat of dissociation of nitrogen; and employed soft X-rays and mass spectrometers to investigate the phenomena occurring in shock fronts. His most recent studies have been in classical chemical kinetics. Honours that have been accorded to him include the American Medal for Merit (1946), the British Medal for Service in the Cause of Freedom (1948), and the Nichols Medal of the American Chemical Society (1947).

As a civilian scientist during the war years, Prof. Kistiakowsky headed the explosives division of the Manhattan Project, was consultant to the Office of Scientific Research and Development, and adviser to the United States Army on scientific problems of a military character. His wide experience and ability have been recognized by his election to membership in the Philosophical Society and the National Academy of Sciences. In recent years, as a member of the President's Scientific Advisory Committee, his activities and interests have been focused on national scientific policy and on science as a force and a balance in international affairs.

Metallurgy at Manchester: Prof. F. C. Thompson

PROF. FRANK CHARLES THOMPSON, who is to retire from the chair of metallurgy and directorship of the Metallurgical Laboratories of the University of Manchester on September 30, will then have served on the Senate of the University for thirty-eight years. Prof. Thompson graduated in the University of Sheffield in 1911 and was awarded the Mappin Medal; he then served on the staff of the University of Sheffield until 1919, after which he held the Royal Society Sorby Research Fellowship at Sheffield for one year before being called to the chair at Manchester.

At Manchester, Prof. Thompson rapidly established himself as a bold leader of research in his own special subject of the plastic deformation of metals and gave detailed consideration to the atomistics of plastic flow at a time when few physicists realized that a meaningful problem existed in this field of study. He also, and perhaps in the long run this is more important, established himself as a wise academic statesman and a truly sympathetic 'father' to his department. It was a paternity which protected and encouraged the younger members of his staff while they went their own way in pursuit of their own problems, and gave to the students a basic sense of security spiced with intellectual challenges. The qualities which served the University so well were unstintingly given to the councils of professional bodies, particularly to the Institute of Metals and the Institution of Metallurgists, and he served as president of both these bodies.

Prof. C. R. Tottle

Charles Ronald Tottle, who is to succeed Prof. F. C. Thompson, graduated in 1941 from the honours school of metallurgy at the University of Sheffield with first-class honours. Joining the English Electric Co., Ltd., he was for some years in charge of the metallurgical laboratories of that firm at Rugby. For five years from 1945 he had academic and teaching experience as lecturer in metallurgy at King's College, Newcastle upon Tyne. From 1950 onwards his experience has been in various branches of the atomic energy field, first as scientist in charge of metallurgical developments at Springfield, where, after promotion to senior principal scientific officer, he was appointed assistant director of the Research and Development Branch. In 1951 he was transferred to the new Culcheth Laboratories, of which, in 1955, he was appointed deputy head. In that year he went to Dounreay as head of research and development, and last year became the deputy director and head of the Reactor Division.

Until 1952, Mr. Tottle's publications were mainly concerned with cast iron and residual stress. Two publications dealt with the plastic flow and deformation of cast iron and a third with the general problem of nucleation of cast metals at the mould face. His more recent contributions have naturally been in the atomic energy field and deal with the effect of alloying elements on the creep of metals and the physical and mechanical properties of niobium and its alloys. Much of his work during this period is still 'classified'.

Botany at Aberdeen :

Prof. James Robert Matthews, C.B.E.

Prof. J. R. Matthews, regius professor of botany in the University of Aberdeen, retires at the end of this session. Students and colleagues alike have much cause to thank Prof. Matthews for the unfailing cheerful encouragement and wise council so freely given over a long and distinguished career. Educated at Perth Academy and the University of Edinburgh, Matthews early displayed a deep interest in taxonomy and ecology which has remained throughout his career and has placed him in the forefront of botanists concerned with the problems of the origin and distribution of plants in Britain. Before his appointment as regius professor at Aberdeen, Matthews served as lecturer at Birkbeck College (1913–16) and at the University of Edinburgh (1920–29) and as professor of botany at the University of Reading (1929–34). During the First World War he contributed to our knowledge of the protozoology of dysentery, serving as a temporary protozoologist at the Liverpool School of Tropical Medicine (Western Command). Matthews has given freely of his time to national and local committees as a member of the Nature Conservancy and for a time as chairman of the Scottish Committee, as chairman of the Macaulay Institute for Soil Research (since 1947) and of the Scottish Horticultural Institute (since 1952). He was elected president of Section K for the Brighton meeting of the British Association in 1948.

Prof. Paul Egerton Weatherley

Dr. P. E. Weatherley, who is to succeed Prof. Matthews at Aberdeen, was born in Leicester and received his early education at Wyggeston School; he gained an open scholarship in natural science to Keble College, Oxford, and graduated in the honours school of botany in 1939. Elected to a Keble research scholarship to study fungal metabolism he acted as a part-time demonstrator. Awarded a Colonial Office Scholarship to the Imperial College of Tropical Agriculture (1940), he obtained the A.I.C.T.A. (1942) and was posted to Uganda in the Department of Agriculture. He was in charge of an experimental farm at one of the government research stations and acted as advisory botanist. There he turned his attention to the problems of water relationships of plants and has pursued this as a major research project on his return to Manchester (1947–49) and at Nottingham since 1949. This has culminated in the design and installation of a highly efficient climatological wind tunnel capable of providing a wide range of precisely controlled environments for growing plants (see *Nature*, 183, 94; 1959). The work has been supported by the Nuffield Foundation and the University of Nottingham. The technique used by Kennedy and Mittler to study the feeding habits of aphids has been applied by Weatherley to study the nature and the movement of solutes in plants. He brings to his new appointment a well knit and vigorously pursued field of experimental botany. Through service on the Board of the Faculty of Science and on University committees, he has acquired at first hand a knowledge of the problems of administration facing universities in this expanding phase of higher education. Apart from botany, Weatherley has a wide range of interests, including painting, hill walking and Scottish country dancing. To his duties as regius professor he brings a wide knowledge of experimental botany, a keen and critical interest in the expanding fields of botany and an appreciation of the difficulties and requirements of students in the modern world of science.

Euratom : British Nuclear Energy Attaché

Mr. D. H. Hill, of the U.K. Atomic Energy Authority, has been appointed resident nuclear energy attaché to Mr. A. H. Tandy, the U.K. Government's representative to the European Atomic Energy Community (Euratom) in Brussels. The Government appointed a permanent representative to Euratom last year. The agreement between the Government and Euratom, which was signed in London on February 4, 1959, provides for close collaboration between the parties for the promotion and development of the peaceful uses of atomic energy within the Euratom community and Great Britain. The nuclear attaché will act as adviser to the British representative and will keep in touch with nuclear developments in all the six member countries of Euratom. Mr. Hill has been a member of the staff of the Authority's Industrial Group since 1956.

Royal Society Artificial Earth Satellites Programme

In accordance with the Prime Minister's announcement on May 12, the Royal Society through its British National Committee on Space Research is engaged in preparing on behalf of the Lord President of the Council a programme of scientific experiments to be carried out in a series of artificial Earth satellites. University departments and other research organizations wishing to propose scientific experiments for incorporation in the programme are invited to communicate with the Assistant Secretary, The Royal Society, Burlington House, London, W.1.

Milk Marketing Board

In 1944 a plan was prepared for an artificial insemination service in all areas of England and Wales except those covered by the pioneer centre that had begun with Cambridge in November 1942. From a 'cow-population' map, territorially convenient blocks of 60,000 cows were ringed off as areas in which to build centres. Centres were to be located on the basis of thirty bulls to each centre (the maximum size because of the risk of foot-and-mouth disease); on the estimate that ultimately 50 per cent of cows in each area would be offered for artificial insemination, and in the belief that 1,000 cows would be inseminated from each bull annually. The last two estimates, thought by many at the time to be far too optimistic, have been confirmed by subsequent history. Already, demand in some areas has resulted in more than ninety cows in every one hundred being inseminated, and the use of bulls is already more than twice the original estimate. In 1959—appropriately the centenary year of the publication of Darwin's "The Origin of Species"—the Milk Marketing Board has announced that 10 million cows have been produced by artificial insemination during the past fourteen years. The way this has been achieved, and the administrative structure of the Milk Marketing Board, is set out in a well-illustrated publication called "Breeding 10,000,000 Cattle" (H.M.S.O.). The Board is rightly proud of its work and tells its story with lively enthusiasm. The fact that a cattle raiser can now breed for a change in the market merely by lifting a telephone is a tribute to the Board and the adaptable British farmer.

New Bell Laboratories

A new laboratory, costing 20 million dollars, will be built by Bell Telephone Laboratories at Holmdel, New Jersey, to meet the expanding need for research and development. Bell Laboratories is the research and development organization for the Bell Telephone System, and employs nearly 11,000 people. The new building will be on a 430-acre site which has been owned by Bell Laboratories since 1929; it has been designed by Eero Saarinen. The first portion of the building is expected to be occupied by late 1961.

Journal of Molecular Biology

This journal is to be published six times a year by the Academic Press, Inc. (London), Ltd. (1, No. 1; April 1959. Subscription £5 per volume), and although published in English, papers in French and German will be accepted. The study of molecular biology attracts scientists from numerous disciplines and with its rapid expansion the problem of correlating results obtained by the specialist has become increasingly difficult. The advent of this new journal with an editorial policy of publishing papers on "the nature, production and replication of biological structure at the molecular level and its relationship to function" should be of great value to workers in this field. With one exception the eight papers and two letters in the first number of the *Journal of Molecular Biology* fall into the framework of molecular biology as defined in the instructions to authors. It is to be hoped that the exception does not represent the thin end of the wedge and that the editors will in future restrict publication to papers dealing with molecular biology and not allow the periodical to develop into another journal of general biochemistry, of which there are already a sufficient number.

The United States National Museum

The annual report of the United States National Museum for 1957–58 (pp. iv+150. Washington, D.C.: Government Printing Office, 1958) records that rapid progress in planning the building for the Museum of History and Technology permitted erection to start in the summer of 1958. The building will be of a rectangular shape having an extended platform to form a terrace at first-floor level. It is significant to note that planning for the interior was undertaken by the architects from draft designs and details submitted by the Museum staff. This is the fifth year of the modernization programme, and the Halls of Health, North American Indian and Eskimos, native peoples of America, and military history have been dealt with. A striking exhibit is that depicting the home life of an average Arapaho Indian family some seventy-five years ago: while the warrior and his wife entertain visitors within a completely furnished tipi, the children play with toys outside and a woman prepares pemmican.

Museum and Art Gallery, Durban

The annual report of the Museum and Art Gallery at Durban for 1957–58 (pp. 19. Durban: Durban Museum and Art Gallery, 1958) states that, in spite of a staff below establishment, much work on display for the public and the re-housing of the scientific research collections has been carried out during the year. The group showing the white-tailed wildebeest and warthog has been re-designed, and work has commenced on the Kruger Park waterhole exhibit. Owing to the vacant keepership in the Art Gallery, work in that branch of the service has been virtually at a standstill, although a few temporary exhibitions have been arranged. In the Old House Museum the court dress and accessories of Sir James L. Hulett have been placed on exhibition, and an interesting tollgate erected in Durban in 1867 has been re-erected in the grounds.

U.S. Atomic Energy Commission: Grants for Training in Radioisotope Technology

Mr. John A. McCone, chairman of the U.S. Atomic Energy Commission, has announced that grants amounting to 251,704 dollars to twelve American colleges and universities will be made for education and training in radioisotope principles and technology. An increase in the number of technical graduates who are able to use radiation as an industrial tool is expected to contribute significantly to the expanding uses of radioisotopes and radiation.

The grants are the first of a series of awards to be made under the Commission's new radioisotope technology training programme. The first series also includes a grant to the University of California, for the purchase of equipment to be used in three industrial radioisotope training courses this summer at Berkeley. Further information can be obtained from the Director, Office of Isotopes Development, U.S. Atomic Energy Commission, Washington 25, D.C.

National Research Council of Canada Support for Universities

INFORMATION about the National Research Council of Canada's current programme of university support for science, engineering and medicine is contained in a "Report on University Support, 1958–59" (pp. ii + 143. Ottawa: National Research Council, 1958. 50 cents), which explains the programme, shows how it is conducted, and lists the recipients of scholarships, fellowships and associateships and the direct grants in aid of research. There is also a list of travel grants. Expenditure on scholarships in 1958–59 is estimated at 490,000 dollars, of which 475,000 dollars is for science and engineering and 15,000 dollars for psychology; on fellowships in science and engineering, 360,000 dollars; in medicine, 100,000 dollars; in dentistry, 12,000 dollars; and on medical associateships, 120,000 dollars. Of the grants in aid of research, 2,350,000 dollars is for science and engineering, and 1,250,000 for medical research; 135,000 dollars is allocated for the Prairie Regional Committee, 400,000 dollars for the Atomic Energy Control Board, 136,000 dollars for associate committees, and 366,000 dollars for general research grants. Grants of 43,000 dollars to assist travel by members of university staffs and of 146,580 dollars for special activities at universities bring the total to 5,908,500 dollars, while of a further 749,500 dollars for indirect university support, including administrative costs of the support programme, estimated at 175,000 dollars, 260,000 dollars are for the publication of the *Canadian Journal of Research.*

University College, London: Report for 1957–58

THE annual report of University College, University of London, for 1957–58 includes the report of the chairman of the College Committee and that of the provost. This gives a brief account of some of the research work in progress, and a full list of publications by members of the College, arranged by faculty and department, occupies 34 pages of the report. Of the 2,827 undergraduate students and 803 postgraduate students 609 and 338, respectively, were in the faculty of science, 201 and 76 in that of engineering and 190 and two in that of medical science. Of the total, 2,943 were from the United Kingdom, 352 from the the British Commonwealth of Nations overseas and 335 from other parts of the world.

Laboratory Animals Centre

THE organization and administration of an animal division for research purposes was considered at a symposium arranged by the Laboratory Animals Centre of the Medical Research Council Laboratories on May 5, 1958. The papers, which have now been published (Laboratory Animals Centre: Collected Papers, Vol. 7; 1958. Pp. 107. Carshalton, 1958. 10*s*.), dealt with the economics and efficiency of an animal division, the relation of an animal division to a research division, the problems of equating supply and demand, the organization of the field laboratories at the University of Sheffield, the scientific research within a laboratory animals division, the staffing of an animals division and animal technician training.

A New Method of Particle-counting on the Electron Microscope

IN making estimates of particle counts by electron microscopy it is necessary for the particles from a known volume to be uniformly distributed over the grid in order to get a random sample of the material. In practice, however, this is difficult to achieve, and Backus and Williams (*J. App. Phys.*, 21, 11; 1950; *J. Amer. Chem. Soc.*, 71, 4052; 1949), as a compromise, have counted all the particles in small droplets, the size of which was determined by the number of polystyrene latex particles known to be contained in a unit volume of the solution. This technique has recently been improved upon by Nixon and Fisher (*Brit. J. App. Phys.*, 9, 66; 1958), who used a high-pressure spray gun made of metal, and intended to work with small droplet sizes; it can be used with as little as 0·2 ml. This decreased the size of the droplet, thus making it possible to use much higher magnifications without sacrificing the ability to obtain a picture of each droplet-trace entire on one frame.

Another approach to the problem has now been made by Dr. D. Gordon Sharp, in collaboration with Ivan Sorvall, Inc., Norwalk, Connecticut, in which virus from a known volume is deposited uniformly over a known area of agar jelly by means of centrifugation. The apparatus consists essentially of a centrifuge rotor with eight numbered compartments and a stainless steel cover. It contains eight stainless steel-housed 'Perspex' cell assemblies, and in each cell is placed a 1 cm. square of 2 per cent agar jelly. 1 ml. of the virus is added to each cell and the rotor spun in the centrifuge at 20,000 r.p.m. After spinning the rotor, the cells are opened and the agar squares, which have the virus particles uniformly distributed on their surfaces, removed to dry. A film of collodion is poured over the agar surface, allowed to dry and floated off on water. The floating collodion is then picked up on an electron microscope grid, and the sample is ready for counting. The advantages of this method seem to be that it is simple to use, and, because there are eight cells, eight different samples can be dealt with simultaneously.

Micro-Spot Cathode-Ray Tube

THE new Ferranti 5/71 *CM* micro-spot cathode-ray tube has a line-resolving power comparable with that of a well-designed lens and marks an important advance in electron optics. The tube can display all the detail that a lens could project on to the same area and can be used to produce equally clear photographic prints. In systems employing the flying-spot scanning technique, however, resolution in the line direction is limited, for a given scanning speed, by the phosphor decay time, and unless this can be reduced without sacrificing light output it will not be possible to take full advantage of the 5,000 lines in such applications.

Hausaland Erg

FROM field work and the interpretation of air photographs, A. T. Grove (*Geog. J.*, 24, 528; 1958) advances the view that the landforms of the plains that stretch along the southern border of the Sahara were shaped by erosion and deposition under climatic conditions that differed greatly from the present, associated with deep weathering, water erosion and the formation of extensive lakes in humid periods followed by phases of much wind action and dune building in the intervening arid periods, matching the alternation of ice and river action in high latitudes. He directs attention, however, to the danger of matching glacial periods with tropical pluvials and to the conflicting views regarding the climatic sequences in the tropics during Pleistocene times in relation especially to the definition, expansion, or movement of the margins of major arid regions such as the Sahara. Much of the key to this fascinating problem may well lie hidden in the ancient Saharan erg and other sand accumulations of the desert fringes.

Injury-feigning Behaviour of Wood-pigeons

DESCRIBED as infrequent in the Handbook of British Birds, two apparently related cases of injury-feigning among wood-pigeons (*Columba palumbus*) have been recorded by C. S. Payne (*The Bedfordshire Naturalist*, 12 ; 1959). Disturbed by a pointer dog in Kempton Park, a wood-pigeon flew straight over the grass at a height of only 1 ft. from the ground, in a manner similar to that of a common sandpiper flying over water. Near the dog was a fully grown and feathered young pigeon which had presumably fallen to the ground before it could fly. Six days later the dog again disturbed an adult wood-pigeon which was "floundering along in the grass as if it had no legs, and progressing a few inches at a time, very awkwardly, by means of its wings". When Payne attempted to pick the bird up it rose buoyantly into the air and flew away. On this occasion no young bird was found. This may have been the same adult which had previously been observed, the distraction behaviour of which had been retained.

Urwick Medal for Management Studies

THE Polytechnic Management Association has instituted a new annual award, to be known as the Urwick Medal, for presentation to the best final-year student in the diploma course in management studies at the Regent Street Polytechnic, London. The first award will be made at the end of the session 1958–59. The Association's members are past and present students of management at the Polytechnic.

Royal Society of Tasmania : Officers

THE following were recently elected to office in the Royal Society of Tasmania for the year 1959 : *President*, The Governor of Tasmania ; *Vice-Presidents*, Mr. L. W. Miller, Dr. D. Martin ; *Council*, Hon. Mr. Justice Crisp, Mr. R. M. H. Garvie, Dr. E. Guiler, Mr. K. D. Nicolls, Mr. M. S. R. Sharland, Mr. J. W. C. Wyett, Mr. W. F. Ellis, Mr. G. H. Stancombe ; *Hon. Treasurer*, Mr. G. E. A. Hale ; *Hon. Auditor*, Mr. A. M. Hewer ; *Hon. Secretary and Librarian*, Dr. W. Bryden ; *Librarian*, Miss E. M. Geddes.

Harwell Reactor School Courses

EIGHTEEN standard or full courses have to date been held at the Harwell Reactor School, and Standard Course No. 19 will start on August 31, and continue until December 18. Altogether, 951 students from 32 different countries have so far attended these courses, which began in September 1954 and are designed to train engineers in the techniques of reactor construction and operation, particularly in connexion with nuclear power stations. Half the places at each course are allocated to overseas students, and a fee of £250 exclusive of accommodation is charged. A special course for senior technical executives will be held during September 21–October 1. This is the ninth course of this kind and the fee is fifty guineas exclusive of accommodation. Application forms and details of both courses can be obtained from The Principal, Reactor School, Atomic Energy Research Establishment, Harwell, Didcot, Berks.

Announcements

PROF. J. A. L. MATHESON, Beyer professor of engineering in the University of Manchester, has been appointed as the first vice-chancellor of the new Monash University, Melbourne.

PROF. N. J. PETCH, professor of metallurgy in the University of Leeds, has been appointed to the chair of metallurgy at King's College, Newcastle upon Tyne. For a note on the work of Prof. Petch see *Nature*, 178, 347 (1956).

MR. A. L. BACHARACH has been elected president of the Nutrition Society in succession to Dame Harriette Chick. Prof. R. G. Baskett, Mr. F. le Gros Clark, Dr. H. N. Munro and Dr. F. Yates were elected ordinary members of Council. Dr. R. J. L. Allen (Beecham Foods, Ltd., Brentford, Middlesex) is honorary secretary.

THE Oliver Bird Prize for 1958 has been awarded to Prof. M. C. Shelesnyak of the Weizmann Institute of Science, Israel, in recognition of his work on the role of histamine in the decidual response of the endometrium and the discovery that ovum-implantation can be suppressed by the presence of histamine antagonists in the uterus before nidation.

A CONFERENCE on Co-operative Phenomena and Phase Transitions, organized by Prof. G. S. Rushbrooke on behalf of the Physical Society, will be held at Kings College, Newcastle upon Tyne, during July 6–7. There will be four sessions, devoted to : thermodynamics and phenomenology ; melting and liquids ; quantal fluids ; and lattice interactions (Ising and Heisenberg models). Further details may be obtained from Miss E. Miles, Physical Society, 1, Lowther Gardens, Prince Consort Road, London, S.W.7.

THE ninth Canadian High Polymer Forum will be held at the Guild Inn, Toronto, Ontario, during October 26–28. The Forum is sponsored by the National Research Council of Canada in co-operation with the Chemical Institute of Canada, and is devoted to all aspects of polymer science. Authors wishing to submit papers for presentation at the Forum should write to the programme chairman, Dr. L. A. McLeod, Research and Development Division, Polymer Corporation Ltd., Sarnia, Ontario, Canada. Titles and abstracts of approximately 300 words will be required by August 1. General information concerning the Forum can be obtained from Dr. M. H. Jones, chairman, Ninth Canadian High Polymer Forum, Ontario Research Foundation, 43 Queen's Park, Toronto 5, Ontario.

THE Australian Branch of the Institute of Physics will hold a Conference on Solid State Physics in Melbourne during August 17–22. Some forty physicists from Australia, four from New Zealand, ten from the United States, about five from the United Kingdom, and two from Canada will read papers on original work. The papers offered fall mainly into the fields of lattice and electron theory of metals, low-temperature physics, imperfections and plastic deformation, crystal growth, and surface phenomena. Other fields of solid state physics will also be discussed. Further information can be obtained from the convener, Dr. W. Boas, Division of Tribophysics, Commonwealth Scientific and Industrial Research Organization, University of Melbourne, Carlton, N.3, Victoria, Australia.

FUNCTION OF THE RUMEN

THE 123rd meeting of the Nutrition Society was held at the Royal Veterinary College, London, under the chairmanship of Dr. D. P. Cuthbertson, director of the Rowett Research Institute, on March 7, when a symposium on "Rumen Function" took place. In his opening remarks the chairman described the theme as one of great fundamental and practical interest where the microbiologist, biochemist, physiologist, animal husbandman, veterinarian, and members of the feeding stuffs trade could meet and learn much through the exchange of knowledge and concepts.

Dr. C. C. Balch (National Institute for Research in Dairying, Shinfield) introduced the subject by describing the structure of the ruminant stomach and the movement of its contents. In the course of its development the ruminant stomach has achieved an efficient microbial digestion of plant fibres and also of practically all other plant constituents, and with this goes the syntheses of microbial polysaccharide and protein and also certain vitamins. The structure of the four portions of the ruminant stomach which emerge from the embryonic stomach —the rumen, reticulum, omasum and abomasum—was described. The abomasum with its typical gastric secretory function corresponds to the stomach of non-ruminants; in very young ruminants it is as large as the rumen.

Co-ordinated movements of the omasum, reticulo-omasal orifice, reticulum and rumen can be recorded pneumatically or seen radiographically. These were described by Dr. Balch.

During eating, the food boli are deposited in the anterior rumen, where they rapidly merge. By the end of a meal of hay most of the new food is to be found tightly packed in the dorsal sac as a relatively dry, fibrous layer, whereas the ventral region will contain a layer of more fluid digesta. The reticulo-rumen never empties, and, in fact, in the stall-fed animal rarely contains less than half its capacity. The amounts found in grazing animals are considerably less. The amount of food given, and especially the amount of hay, is a major factor influencing the length of time residues remain in the rumen: there is a slight tendency for concentrates and succulents to pass out of the reticulo-rumen more rapidly than roughages. According to Gordon, the onward passage of particles of hay is greatest during rumination. The transfer of digesta to the omasum is a continuous process.

Dr. B. H. Howard (Rowett Research Institute, Aberdeenshire), in his contribution on the metabolism of carbohydrates by rumen bacteria, first described the various techniques which have been used: (1) *in vivo* studies; (2) 'artificial rumen' preparations; (3) washed cell suspensions; (4) direct microscopic observation including use of fluorescing antibodies; (5) pure culture; and (6) 'enrichment culture' experiments.

Cellulose is the most important of the polysaccharides fermented in the rumen, and xylan occurs in close association with it. Most of the rumen cellulolytic and xylan-decomposing bacteria are very strict anaerobes and some require carbon dioxide and/or rumen liquor. Cellulose yields mainly acetic, lactic and succinic acids in pure culture fermentations, and xylan gives fatty acids, from formic to butyric. Mixed rumen organisms, on the other hand, convert both substances mainly into varying proportions of acetic and propionic acids.

The main rumen starch-fermenter is *Streptococcus bovis*, chains of cells of which can be seen attached to decomposing starch grains. It produces only an α-amylase, and lactic and acetic acids are the chief fermentation products. The same organism will also ferment the oligo- and poly-saccharides containing fructose, found in grass and root crops.

Rumen micro-organisms show a striking capacity to synthesize polysaccharides either internally as iodophilic deposits of 'starch-like' material, or externally as capsules or slime-layers. It is doubtful if the material leaving the rumen to enter the omasum contains any significant amount of digestible carbohydrate of microbial origin.

Lactic and succinic acids added to the rumen are quickly decomposed, yielding mainly propionic acid. Rumen acetic and butyric acids are interconvertible. Formic acid is rapidly decomposed in the rumen to carbon dioxide and hydrogen, which further react to give methane; some five rumen-volumes per day arise from this reaction normally.

In his paper on the utilization of protein by the dairy cow, Dr. M. J. Head (National Institute for Research in Dairying) said that as a result of the action of the ruminal micro-organisms, the value of the nitrogenous moiety of the feed to the dairy cow is not so dependent on its amino-acid structure or its proportion of true protein as is the case with a single-stomached animal. The ammonia produced during the fermentation is either utilized for the growth of organisms which are later digestod to give nutrients of high biological value, or is absorbed through the rumen wall into the blood-stream and largely wasted. This loss has not been sufficiently considered in evaluating protein feeds for ruminants.

The classical assessment of the biological value of a protein is complicated in the case of a ruminant by the fermentation in the rumen, as has been shown by the work of Chalmers and Synge. The greater the loss of ammonia from a protein, the greater the significance to the animal of the amino-acid structure of the feed protein residues leaving the rumen unattacked.

A comparison of the various oil-cake residues normally used as protein sources for dairy cows on the basis of daily *in vivo* rumen ammonia concentration curves did indicate differences between the cakes. A similar classification of these protein sources could be made on the basis of the proportion of their total nitrogen soluble in 1 *M* sodium chloride solution.

While theoretically the most desirable type of protein for a ruminant is one of low solubility in the rumen and yet of high biological value for a single-stomached animal, two further questions need consideration with reference to practical feeding. First, is the dairy cow normally rationed sufficiently stringently for any of these theoretical improvements to be seen to advantage; and secondly, may it not be more economic to feed a theoretically wasteful protein source if it still supplies cheaper units of biological value ?

In discussing lipids in relation to rumen function, Dr. G. A. Garton (Rowett Research Institute) prefaced his paper by a consideration of the nature of dietary lipids. The lipids present in feeding stuffs such as grass, hay, silages and concentrates were considered with special reference to the C_{18} polyunsaturated fatty acids (linoleic and linolenic) which form a large part of the total fatty acid content.

Events in the rumen were considered first with reference to the hydrogenation of unsaturated fatty acids, which occurs to a considerable extent under the influence of the rumen bacteria. This results in the production, *inter alia,* of stearic acid which, following intestinal absorption and deposition, may well account for the characteristic 'hardness' of ruminant depot fats.

Recent findings on the hydrolysis of triglyceride fats in the rumen by a bacterial lipase were then outlined. These demonstrate that most of the fatty acids entering the rumen as glycerides reach the abomasum and small intestine in the free state—a situation markedly different from that in monogastric animals in which partial lipolysis takes place in the small intestine. The fermentation of the liberated glycerol (to yield propionic acid) was briefly discussed.

The ruminant does not appear likely to derive any of the so-called 'essential' fatty acids from the lipids of its rumen bacteria. Thus it appears that, if the ruminant requires 'essential' fatty acids, they must be of dietary origin and must also escape hydrogenation in the rumen.

In his contribution on milk composition in relation to rumen metabolism, Dr. J. A. F. Rook (National Institute for Research in Dairying) indicated that the observations of Powell in 1938–41 provided convincing evidence that the fine grinding of the entire roughage in a ration or, alternatively, a considerable reduction in roughage intake and an increase in the concentrate feed, reduced the percentage and yield of fat without affecting total milk production. This specific effect on fat secretion has been fully confirmed by Balch, Balch, Bartlett, Cox and Rowland at Shinfield. Milk of unusually low fat content was observed by McClymont to result from cows grazing on young herbage or fed on kale, concentrates and limited amounts of hay or straw, that is, diet short of roughage. The operative factor is the physical condition of fibrousness rather than the presence of fibre.

The depression in the milk fat secretion of cows on low roughage diets has invariably been associated with a change in fat composition. Milk fat in the cow and other ruminants is distinguished from the milk fat of other species, and from animal depot fats in general, by a relatively high content (up to 20 per cent on a molar basis) of short-chain (C_2–C_{10}) acids, and when a reduction in fat secretion occurs the proportion of these acids is correspondingly reduced. Some reduction in the weights of higher saturated (largely palmitic and stearic) and also unsaturated (largely oleic) acids secreted is also observed.

Additions of sodium acetate (500–1,500 gm./day) or acetic acid have produced an almost complete recovery in the fat content of milk, but individual animals have failed occasionally to show a response to sodium butyrate. It is held to be the change in the production of acetic and propionic acids that has generally been responsible for the depression in milk fat synthesis.

The role of the protozoa was outlined by Dr. Margaret Eadie (Rowett Research Institute) in her paper on some aspects of rumen ciliate protozoa. According to Dr. Eadie, the basic nature of the association of rumen ciliates with rumen function is a complex one still not clearly understood, but their study is valuable because of the one justified generalization: that certain species of ciliates have been found in the rumen of all normal adult ruminants so far examined.

In general, diet appears to have the greatest effect upon the ciliate population, and variations are so large that no acceptable average figure can be given nor can the ciliate protein contribution be accurately assessed. This may be as high as 20 per cent of the total host requirement, and qualitative studies have indicated that the ciliate protein is of higher nutritional value than the rumen bacterial protein.

Comparisons of faunated and non-faunated animals have so far shown no serious effects on those free from ciliates, but it has yet to be ascertained whether advantage from a ciliate population would appear under conditions of stress. In recent work in collaboration with Dr. Preston at the Rowett Institute, experiments are in progress to determine, by variation of the roughage content of the weaning ration, how soon ciliates may be permanently established in early-weaned calves and whether this is advantageous.

Numerically the oligotrich organisms, particularly *Entodinium* spp., make up the largest proportion of most populations. So far, the holotrichous organisms, which are fewer in number, have been most closely studied and the information of the biochemical and nutritional properties of these organisms suggests that equally interesting information should accrue from similar studies of the oligotrich ciliates.

In his paper on the treatment and prevention of bloat with anti-foaming agents, Mr. C. S. W. Reid (Plant Chemistry Division, Department of Scientific and Industrial Research, Palmerston North, New Zealand, at the Physiological Laboratory, Cambridge) pointed out that if stable foams are generated during fermentation, the elimination of gas from the rumen is impeded and bloat (tympanites) may result. His paper reviewed work carried out in New Zealand on the use of anti-foaming agents in the treatment and prevention of acute bloat in grazing dairy cattle. Administration of foam-breaking substances—fats and oils, certain detergents and other surface-active materials but not silicones—was the only consistently useful treatment found. Materials at present recommended for field use are peanut oil and emulsified ruminant tallow in doses of 120–150 gm. fat. Anti-foaming agents were also effective when given prophylactically. Pasture spraying proved to be a reliable control measure and has been used on New Zealand farms over four seasons. It has also been notably successful in preventing bloat on irrigated pastures in Australia.

Detectable anti-foaming activity is present in the rumen contents and can be shown to be affected by the activity of the micro-organisms. However, apart from indicating the probable complexity of the situation, observations so far have not revealed obvious correlations between lipid intake, anti-foaming activity and bloating.

Dr. A. T. Phillipson (Rowett Research Institute) in his paper on the rumen in relation to the animal considered first the extent of digestion in the reticulum and rumen. He pointed out that several estimates have been made of the extent of digestion in the reticulum and rumen which are based on the lignin ratio and which suggest that the quantity of food constituents disappearing ranges from 43 to 83 per

-cent in cattle and that a similar but rather narrower range has been found in sheep. Most of the material disappearing is carbohydrate. It is more difficult to assess the extent of disappearance of nitrogen-containing materials as the secretions augment the nitrogen of the food, but it appears that considerable losses occur from the rumen in both cows and sheep and presumably these represent the absorption of ammonia. However, losses in the intestine are more extensive when compared with the apparent digestibility of nitrogen for the whole alimentary tract.

Estimates of fatty acid production in the rumen show that they are quantitatively important. The recent work of Armstrong and Blaxter at the Hannah Dairy Research Institute indicates that at levels of feeding up to maintenance the value of the mixture of short-chain fatty acids to the animal as a source of energy is fairly constant irrespective of the quantities of each individual acid absorbed. For production purposes, rations that favour the formation of propionic and butyric acids should be more valuable than those that favour the production of acetic acid. The proportions of propionic and butyric acids increase as the concentrate part of the ration increases in cattle. In particular, starch-rich food increases the proportion of propionic acid. As yet, very little is known of the peptic and intestinal phases of digestion.

In the second part of his paper, Dr. Phillipson dealt briefly with the absorptive capacity of the intestinal tract. One of the conditions of terrestrial life is the necessity of conserving water and sodium, and the ruminant is unusually good at carrying out these two tasks.

The quantities of water and sodium secreted in the saliva alone are far greater than the quantities excreted in the faeces. The contribution made by other digestive juices still needs investigation and is likely to be considerable. Both sodium and water are known to be absorbed from the rumen and omasum, while there is no doubt that absorption also occurs along the remainder of the tract, particularly in the large intestine. It is of particular interest that in conditions of sodium depletion the sodium content of the saliva is lowered and its place is taken by potassium ; there is also a diminution of the volumes secreted. A study of the rates of turnover of body constituents such as water, sodium and other elements and nitrogen in various circumstances may help in the end to understand why occasionally things go wrong.

The final paper of the symposium was by Mr. J. K. D. Dow (Unilever, Ltd.) on the application of recent scientific information through the feeding-stuffs industry.

Studies on the absorption of fatty acids in the rumen, and the connexion with hormone metabolism, indicate dietary means of regulating milk production and quality and of curing conditions such as ketosis. Chemical tests enable processed protein materials to be classified according to the needs of the animals for which they are best suited. The feeding-stuffs industry has already made use of research into the vitamin and mineral requirements of ruminants. Further research on the effect of these on roughage utilization is awaited.

Recent work on antibiotic supplements for calves has indicated results which are not applicable through the industry in the present stage of legislation. This case demonstrates the wide view which is demanded of the research worker to-day, particularly when some manufacturers may depend entirely on published scientific evidence in formulating new feeding stuffs. However, it is doubtful whether fundamental research workers have adequate facilities for testing their results under practical conditions. This problem offers a profitable field for consideration by the feeding-stuffs industry, because co-operation between the research worker and the manufacturer is essential to the efficient functioning of the industry and, ultimately, will ensure that the farmer reaps the fullest benefit.

D. P. CUTHBERTSON

NUCLEAR FUEL CYCLES

THE Institute of Physics, in collaboration with the British Nuclear Energy Conference, held a symposium on "Nuclear Fuel Cycles" at the Institution of Civil Engineers, Westminster, on January 22 and 23. The symposium was opened by the president of the Institute of Physics, Sir George Thomson, who welcomed some 250 members and visitors, including delegates from eight European countries. He stressed the importance of fuel cycles in relation to the large nuclear power stations now under construction in the United Kingdom. These would prove competitive with coal-fired stations only if their uranium fuel were employed in the most efficient manner.

The symposium was divided into three sessions, the first of which considered the basic physics of long-term reactivity changes and nuclear fuel cycles, the second was concerned with the optimization of fuel cycles, and the third session discussed relevant operational problems. The chairman of the first session was Dr. J. V. Dunworth (Atomic Energy Research Establishment, Harwell). The first paper presented was that by Dr. H. Rose and Mr. J. J. Syrett (Atomic Energy Research Establishment, Harwell) on "Long-term Reactivity Changes", which described the basic physical processes occurring as natural or slightly enriched uranium is irradiated in large graphite-moderated thermal reactors. The importance of these changes was emphasized since, together with considerations of metallurgical damage, they would determine the irradiation-level at which the fuel must be replaced. The overall reactivity-changes with irradiation are determined mainly by the small net difference between the large changes arising from the burn-up of uranium-235 and the formation of plutonium-239, making the problem unusually sensitive to all the relevant nuclear data. Furthermore, the plutonium isotopes formed in the irradiated uranium have large resonances in their fission and capture cross-sections at low neutron energies. The prediction of their rates of reaction with neutrons therefore demands a detailed knowledge of neutron spectrum conditions to an extent unnecessary in assessing the initial reactivity of the reactor. For these reasons, present predictions rely considerably upon integral measurements which are made on irradiated fuel elements. Much of this work has been carried out using the *Gleep* pile oscillator at Harwell, where data have been accumulated from uranium which has been highly irradiated in the Windscale, NRX and Calder Hall reactors. Typical predictions were displayed of the long-term reactivity changes to be expected for an individual fuel element in the Calder Hall type reactor, and the dependence of the reactivity curve upon several important design parameters was also illustrated.

In the ensuing discussion, Mr. P. W. Mummery (Atomic Energy Research Establishment, Harwell) explained that the long-term reactivity changes occurring at Calder Hall have been observed directly. Their interpretation was difficult since they applied to a complete reactor, and it was necessary to allow for the effects of different irradiation-levels throughout the reactor and the variation with irradiation of the control-rod effectiveness. Even so, there were some grounds for satisfaction that these measurements were in reasonable agreement with the *Gleep* experiments. Finally, he emphasized the very high accuracy on the basic nuclear data which is demanded for a purely theoretical approach to these problems.

For a given flux distribution and fuel-cycle scheme, the long-term reactivity changes of an entire power reactor may be found by suitably weighting the contribution from each fuel element. This was discussed in the second paper, by Mr. S. E. Lewis (Nuclear Power Plant Co. Ltd.). He considered the basic theory of 'once-through' fuel cycling, in which the fuel supplied to the reactor has a constant composition and does not contain any materials produced during the irradiation of previous charges. Mr. Lewis showed how an equilibrium state is reached in a small region where the flux is uniform and maintained constant, and demonstrated the factors determining the reactivity of the region and the whole reactor during the approach to the equilibrium state. The equilibrium state is determined when fuel is added and removed continuously in such a way that in any region of the reactor all irradiation-levels are represented between zero and the maximum allowable. Certain basic fuel-cycle schemes were outlined, some of which necessitated fuel movement within the reactors. It was concluded that the delay of commencement of continuous fuel replacement could be economically advantageous, and warranted closer study.

It is necessary to investigate the local behaviour of reactor flux and heat output in the small region considered in the previous paper, as the fuel elements will have different irradiation histories. This problem was discussed in a paper on perturbations due to fuel cycles which was presented by Dr. J. G. Balfour, Dr. D. L. Booth and Mr. R. S. Bulloch (Atomic Power Projects). One-group perturbation theory was applied to the calculation of axial flux changes in a single channel caused by the non-uniform irradiation and temperature, and by axial fuel shuffling within the channel. An improved method was then developed in which the non-linear one-group diffusion and heat transfer equations were solved numerically, this being applicable even when the perturbations were large. Axial distributions of flux and of coolant temperature were illustrated both before and after neutron irradiation of the fuel. A final section of this paper described the use of the Feinberg method for estimating local channel-to-channel variations of power and flux during a continuous fuelling scheme. The work suggested that although the fission cross-section of a fuel element varied considerably over its life due to build-up of plutonium, the heat output maintained a more constant level due to the increased depression of the neutron flux.

In the discussion, Mr. Syrett pointed out that the choice of fuel cycle had an important bearing upon reactor economics. In the approach to equilibrium which lasted several years, large sums of money could be saved by a judicious choice which would reduce fuel requirements and investment charges. He explained the potential advantages of radial shuffling for giving improvements during the approach period and in the equilibrium state.

In summing up the session, the chairman emphasized the importance of reaching a practical and economic fuel-cycling procedure for the Central Electricity Generating Board reactors, one which would have to take into account many different technologies. It was imperative that during the first few years of operation of these reactors, intensive operational research should be performed to improve our knowledge of fuel-cycling problems.

The second session (chairman, Mr. L. Rotherham of the Central Electricity Generating Board) contained two papers concerned with the optimization of fuel cycles. The first, by Mr. P. R. J. French and Mr. C. S. Lowthian (A.E.I.–John Thompson Nuclear Energy Co. Ltd.), considered a once-through equilibrium fuel cycle. The influence of the fuel cycle on the optimization of the reactor design through the lattice parameters was studied, and a relationship developed between burn-up of fuel and the initial neutron spectrum conditions. The effect of enrichment upon fuel life was also discussed, together with the allocation of excess reactivity to increase reactor output or fuel life.

The second paper was presented by Dr. P. J. Grant, Mr. W. Oswald and Mr. P. D. D. Russell (General Electric Co. Ltd.) This examined economic factors affecting the choice of fuel cycle for nuclear power stations, and underlined certain aspects often overlooked. Optimization of the fuel cycle is only a part of the overall optimization of cost per kilowatt hour, which depends partly upon local conditions. Neutron economy was important, but might sometimes conflict with monetary economy. As an example, flux flattening with steel absorbers and attendant loss of neutrons at the reactor centre could yield longer fuel life and reduce power costs. The economy of enrichment, plutonium production and fabrication costs was considered, as were the present prices of nuclear fuels. The advantages of axial fuel shuffling in the Calder Hall type reactor, and the necessity for continuous charge and discharge schemes, were also discussed. It did not appear generally economic to reduce deliberately the irradiation-level below the metallurgical limit.

Mr. G. E. Darwin (Babcock and Wilcox Ltd.) commented in discussion on the importance of this limit. The uranium and canning materials would not stand up well to fuel shuffling and the necessity to operate under differing physical conditions. This would result in reduced metallurgical limits depending upon the shuffling schemes, and it was inadvisable to assume a constant limit in fuel-cycle considerations. Mr. Syrett pointed out that delaying the onset of the equilibrium charge – discharge scheme could reduce fuel requirements, and since potential savings of the order of £1 million per reactor were possible this provided an incentive for such schemes. He asked Mr. French and Mr. Lowthian whether large computer programmes were preferable to their analytical approach to fuel cycle considerations. Mr. Lowthian replied that it might be difficult to analyse all the information provided by the machines, but agreed that machine effort was extremely useful. In response to a question by Dr. G. Davis (Israel), Mr. Mummery stated that one could not dismiss fuel cycling and on-load charge – discharge machines as luxuries, since these provided a potential reduction of the order of a factor of two in fuel costs as well as making it possible to discharge burst cartridges without losing output.

A paper on the operational problem associated with fuel cycling was presented by Mr. J. C. C. Stewart and Dr. N. L. Franklin (Risley) in the third session, for which Prof. J. Diamond (University of Manchester) was in the chair. The authors pointed out that unlike some other industries, conservative operating procedures based upon precisely specified codes of practice cannot be expected because of the rapidity of development in the reactor field. It is essential in their opinion to choose an irradiation life-time which represents a compromise between metallurgical failure-rate and reduction in fuel costs. Sums of the order of £1 million per charge might depend upon this choice. They believed that the reactor operator and fuel manufacturer must carry out a sequential experiment to study the development of fuel cycles and ultimate life of fuel elements, using the actual power reactor itself as the test vehicle. This would also allow for the introduction and testing of subsequent types of fuel element as they are developed. The authors pointed out that this would have considerable influence upon the fuel fabrication facilities required.

Dr. C. P. Haigh (Central Electricity Generating Board) remarked that as a reactor operator he had special problems to consider such as on-load refuelling. The high capital costs of reactors had to be offset by low fuel costs and a high load factor. Shut-down of one reactor for one day would cost £8,000, while a prolonged shut-down involving a complete fuel discharge would cost around £2 million. Thus the reactor operator must be somewhat conservative initially in relation to fuel cycling. Experience would be accumulated gradually on reliability, before large-scale use would be made of complex fuelling schemes.

The closing remarks at the end of the symposium were made by Mr. P. W. Mummery, who explained that the main aim of the symposium had been to indicate the implications of the basic physics problems involved in nuclear fuel cycles on the design and operation of reactors. Compromises are necessary between conflicting requirements from many fields such as physics, metallurgy, engineering, heat transfer, operational simplicity, etc. The potential advantages of various types of fuel cycle had been indicated, on the assumption that various kinds of fuel movement within the reactor were possible and that the irradiation life was limited only by reactivity. Although such cycles could not be used initially, until more experience and more information had been gained, the design of reactors should be flexible to allow for developments such as these. It would be many years yet before the best fuel cycle was established for the Calder Hall type reactor. He looked forward to a time, three or four years hence, when actual operating experience of fuel cycling on different systems might be reported at a similar symposium.

The papers presented at the symposium and a summary of the important discussion will be published in the July issue of the *Journal of the British Nuclear Energy Conference*.

H. Rose

THE ROYAL AERONAUTICAL SOCIETY

AWARDS FOR 1958

THE following awards have recently been made by the Royal Aeronautical Society: *Honorary Fellowship* has been conferred on Prof. J. Ackeret (professor of aerodynamics at the Federal Technical College, Zurich), Sir William S. Farren (technical director, A. V. Roe and Co., Ltd.), S. B. Gates (chief scientific officer and consultant to the director of the Royal Aircraft Establishment); *Honorary Companionship* has been conferred on E. C. Bowyer (director and chief executive of the Society of British Aircraft Constructors), Sir William Hildred (director-general of the International Air Transport Association).

Silver Medal of the Society has been awarded to Dr. E. A. Watson, director of Joseph Lucas (Gas Turbine Equipment), Ltd., for his achievements in the development of turbine engine combustion and fuel systems; *Society's Bronze Medal* to D. G. King-Hele, of the Royal Aircraft Establishment, Farnborough, for his contributions to Earth satellite orbital theory; *British Gold Medal for Aeronautics* to R. S. Stafford, technical director, Handley Page, Ltd., for his outstanding practical contributions to aircraft design; *British Silver Medal for Aeronautics* to D. J. Farrar, chief designer, Guided Weapons, Bristol Aircraft, Ltd., and Dr. N. H. Searby, manager, Guided Weapon Research and Development, Ferranti, Ltd., for their practical contributions to the development of guided weapons; *Wakefield Gold Medal* to K. A. Wood, superintendent in charge at the Atomic Weapons Research Establishment, Orfordness, for his practical achievement in the development and application of electronic aids to all-weather approach and landing; *R. P. Alston Medal* to A. W. Bedford, chief test pilot, Hawker Aircraft, Ltd., for his contributions to the technique of flight testing high-speed aircraft; *N. E. Rowe Medal*, for the best lecture given before any branch by a member of a branch, to J. Dunham, Rolls-Royce, Ltd., for his paper on "Damage to Axial Compressors" given before the Derby branch of the Society; *Simms Gold Medal* to Mr. R. P. Probert, deputy director, Engine Test Facilities, National Gas Turbine Establishment, for his paper on "Ram-Jets"; *George Taylor (of Australia) Gold Medal* to Mr. H. L. Cox, of the National Physical Laboratory, for his paper on "The Application of the Theory of Stability in Structural Design"; *Edward Busk Memorial Prize* to Mr. T. R. F. Nonweiler, of The Queen's University, Belfast, for his paper on "The Man-powered Aircraft

—a Design Study"; *Orville Wright Prize* to D. A. Spence, of the Royal Aircraft Establishment, Farnborough, for his papers, "The Lift on a Thin Aerofoil with a Jet-augmented Flap" and "Some Simple Results for Two-dimensional Jet-flap Aerofoils"; *Herbert Ackroyd Stuart Memorial Prize* to Mr. A. A. Lombard, director of engineering, Aero-Engine Division, Rolls-Royce, Ltd., for his paper on "Thinking about Aircraft Engines"; *J. E. Hodgson Prize* to Mr. J. E. Allen, head of Aerodynamics, Project and Assessment Department, Weapons Research Division, A. V. Roe and Co., Ltd., for his paper, "From Aviation to Astronautics"; *Branch Prize* to Mr. B. D. Blackwell, engineering manager, Bristol Aero-Engines, Ltd., for his paper on "Some Investigations in the Field of Blade Engineering"; *Navigation Prize* to Mr. C. M. Cade, of the Research Department of Kelvin and Hughes, for his paper on "Radio-Astronomy and Navigation"; *Usborne Memorial Prize* to Dr. J. S. Przemieniecki, of Bristol Aircraft, Ltd., for his paper on "Matrix Analysis of Shell Structures with Flexible Frames"; *Pilcher Memorial Prize* to Mr. A. W. Kitchenside, of Vickers-Armstrongs (Aircraft), Ltd., for his paper on "The Effects of Kinetic Heating on Aircraft Structures".

NEW NATURE RESERVES IN BRITAIN

THE Nature Conservancy has recently announced the establishment of four new nature reserves and one forest nature reserve.

The Rhinogs Nature Reserve. The Harlech dome and its borders display the thickest succession of Cambrian rocks to be seen in Britain. It forms a region of desolate and almost uninhabited moorland with high, rugged block-like mountains where the Rhinog Grits break the surface. The two principal peaks are Rhinog Fawr (2,362 ft.) and Rhinog Fach (2,330 ft.). The new reserve covers two blocks of these uplands, lying on either side of Bwlch Drws Ardudwy about five miles east of Harlech, which together total about 991 acres; it is hoped that it will ultimately be extended to include other areas of outstanding scientific interest in the area. The first of these blocks comprises the northern slopes of Rhinog Fawr from the peak down to about 1,066 ft., and the second includes the peak and north-eastern slopes of Rhinog Fach down to the 1,000-ft. contour. The terrain is rugged and wild in the extreme, with a considerable amount of exposed rock in the form of steep crags, broken slopes and block screes. A flock of wild goats, thought to be of domestic origin, frequents the Bwlch Drws Ardudwy area, and pine martens have been seen there in recent years.

Compared with other parts of Snowdonia, the Rhinogs are relatively lightly grazed by sheep, and this may be related to the abundance and luxuriance of heather which extends on these hills from about 600 ft. to the summits. The rocky, well-drained slopes up to the 1,500-ft. contour are covered with dense heather, mixed here and there with bilberry, both reaching 5 ft. in height in the more sheltered situations. The less rocky well-drained areas bear patches of acidic hill grassland, mainly of the *Agrostis–Festuca* type, with some bracken. Wherever hollows and stream flushes occur small bog patches are found, and the wettest ground is occupied by blanket bog with peat up to 4 ft. deep. The small summit plateaux and the steep craggy uppermost slopes of the two Rhinogs bear much block scree, and here the heath forms dense prostrate mats with unidirectional growth away from the prevailing south-west winds.

Access to the reserve is unrestricted, but those wishing to collect specimens or to carry out research should apply for permits to the Regional Officer for North Wales, The Nature Conservancy, Y. Fron, The Crescent, Upper Bangor, Bangor, Caernarvon.

Coed Dolgarrog Nature Reserve, which lies about seven miles south of Conway, is an excellent example of an oak wood on the drier north-eastern side of Snowdonia; many of the trees are intermediate in kind between the sessile and pedunculate oak. Viewed from the floor of the Conway Valley, these woods are probably the most impressive in North Wales; they clothe a precipitous slope which falls from 1,000 to 100 ft. It is unlikely, because of the topographical features of the area, that the woods have been subjected to any form of intensive land use. The reserve, most of which lies within the Snowdonia National Park, covers 170 acres and has been established under a lease from the Central Electricity Generating Board.

Coed Dolgarrog is of particular interest ecologically because of the variety of underlying rocks and the clarity with which their effects on the vegetation are displayed. The central part of the wood lies on lime-rich volcanic ash and has a luxuriant ground flora including much dog's mercury, slender false-brome and sanicle. At higher altitudes elsewhere in Snowdonia this particular kind of rock bears a rich arctic–alpine flora which makes Cwm Idwal and other parts of the district of great botanical interest. The southern and northern portions of the wood, on a hard acidic rhyolite, present a striking contrast, having a grassy ground flora often associated with bracken and sometimes with short bilberry and mosses.

Also included within the reserve are the Ardda alder woodlands, which extend along the northern bank of the Afon Ddu and represent an extension of Coed Dolgarrog into the upland country beyond the steep valley slopes of the Conway. This section is at a higher altitude, being between 750 and approximately 850 ft., with a correspondingly higher annual rainfall—about 60–70 in. as compared with 50 in. for the main body of Coed Dolgarrog. The woods occupy a gently sloping upland valley, which is thickly covered with glacial drift. Soils of impeded drainage are widespread, hence the abundance of the alder and plant communities of wet soils. These woods have escaped clearing from the sixteenth century onwards because the valley in which they grow is extremely inaccessible and the pressure of land use has been correspondingly smaller throughout the centuries. They are of particular interest in the study of the alder at a relatively high altitude.

Permits will be necessary for those who wish to undertake research, to collect specimens, or to visit areas away from the rights of way. Applications for permits should be sent to the Regional Officer for North Wales, in Caernarvon.

Coed Gorswen Nature Reserve, lying at the northern end of the Conway Valley on the western side of the river near Rowen, is a good example of a lowland oak wood. The reserve, which covers 33 acres of the woodland and lies within the Snowdonia National Park, has been established under leases with the owners of the land.

The subsoil of Coed Gorswen is a very bouldery glacial drift and probably as a consequence of this it has been woodland for a very long time, perhaps throughout the historical period. The oaks consists of a heterogeneous population of intermediate forms between the sessile and pedunculate oak. As well as oak, other trees present in some quantity include elm, ash and alder. The ground flora is typical of rather base-rich soils, including such species as dog's mercury, sanicle, slender false-brome, common enchanter's night-shade, broad helliborine, skull cap and very locally yellow archangel. Fringing the wood is some interesting fenny ground—no doubt the "gors wen" (white marsh) which gave the wood its name—dominated by purple moor-grass with associates such as quaking grass.

Permits, which will be required to visit parts of the reserve away from the rights of way, to collect specimens of animals or plants, or to undertake research, can be obtained from the Regional Officer for North Wales.

Allt Rhyd-y-groes Nature Reserve is situated in the valley of the Afon Doethie, a tributary of the Towy, about nine miles north of Llandovery in Carmarthenshire. The reserve consists of 46 acres of oak woodland and has been leased to the Nature Conservancy by the Earl of Cawdor. It is hoped that it will ultimately be extended to include other areas of outstanding scientific interest in the locality.

The reserve overlies shales of Silurian age, and extends between 500 and 1,000 ft. on the west side of the steep flanks of the Doethie Valley. The woodlands are dominated by the sessile oak, as is the Coed Rheidol Nature Reserve in Cardiganshire, but here at Allt Rhyd-y-groes a number of the trees are well grown and display a vigour which is not often seen in equivalent woods elsewhere in Wales. The drier, more eroded slopes are clothed in sweet vernal grass together with mosses at the lower levels, and sheep's fescue higher up the slope.

Permits to visit parts of the reserve away from the rights of way, to collect specimens of animals or plants or to undertake research, can be obtained from the Regional Officer for South Wales, The Nature Conservancy, c/o Department of Zoology, University College of Swansea, Singleton Park, Swansea.

Blackcliff and Wyndcliff Forest Nature Reserve. An agreement has recently been reached between the Nature Conservancy and the Forestry Commission on the management of approximately 200 acres of Blackcliff and Wyndcliff Woods, forming part of the Commission's Tintern Forest, Monmouthshire, as a Forest Nature Reserve in the interest of nature conservation and ecological research jointly with those of timber production. The high amenity value of the area, which is close to Tintern Abbey and within the Forest of Dean Forest Park, will be maintained. These woods, situated on the Carboniferous limestone of the Wye Valley, have long been regarded by botanists as being of outstanding scientific interest; they were visited by John Ray in 1662 and by Sir Joseph Banks and John Lightfoot in 1773. The steep slopes are finely wooded with ash, wych elm, beech, small-leaved lime, yew, oak, cherry and whitebeam and service tree, together with a number of shrubs including dogwood, guelder rose and spurge laurel. The ground flora is rich and includes some locally uncommon species: lily of the valley is found there, and white angular Solomon's seal occurs on the cliffs.

Access will be unrestricted, but permits will be required to collect specimens of animals or plants, or to undertake research. Applications for permits should be sent to the Regional Officer for South Wales at the University College of Swansea.

INVESTMENT IN THE COAL, ELECTRICITY AND GAS INDUSTRIES

IN replying for the Government in a debate on fuel and power policy in the House of Commons on February 6, the Parliamentary Secretary to the Ministry of Power, Sir Ian Horobin, said that the oil companies and the Central Electricity Generating Board were considering together whether, within the framework of existing contracts, it would be practicable to postpone the conversion of two more power stations to oil during 1959; even in the changed industrial climate of the past twelve months Sir Ian said it would be wrong and improper to break contract or use pressure to that end. In moving the second reading of the Electricity (Borrowing Powers) Bill on January 20, the Paymaster-General, Mr. R. Maudling, said that the purpose of the Bill was to increase the authorized capital of the industry under the Bill, and the Electricity Council's permitted borrowings would be increased to £2,300 million, those of the North of Scotland Hydroelectric Board to £300 million and of the South of Scotland Electricity Board to £135 million. The total capital investment of the industry envisaged over the next seven years amounted to £2,130 million, of which £1,470 million would be in generation and £660 million in distribution: these figures were for the Electricity Council alone. This plan was based on estimated demand for electricity over the period, including a two-thirds increase in consumption, in which farm uses would be doubled and other commercial use would increase by about 50 per cent, or an annual increase of 6·6 per cent compared with 7·6 per cent in the past seven years. To meet this estimated increased demand of just under 9 million kilowatts, new plants for 12·25 kilowatts would be commissioned. The load factor had improved from 42·7 per cent in 1947 to 46·8 per cent in 1958 compared with a probable maximum of 60 per cent, and the problem of increasing the factor was being tackled with vigour. The cost per kilowatt of increased capacity was now no higher than ten years ago, in spite of the increase in cost of materials and labour. As regards nuclear power, the cost of the Bradwell and Berkeley stations would be about three times that of a coal-fired station, but that of Hinkley Point should be about 2·5 times, and it was now calculated that this would be about £120 a kilowatt. By the nineteen-sixties the nuclear plant should be marginally more economical than conventional plant. There had already been a reduction at the rate of about 3 million tons of coal a year in the amount of oil to be used for power stations in the early nineteen-sixties, and the Government believed that the demand of the power stations for coal would rise throughout the next seven years.

Lord Mills, the Minister of Power, added a few further details in moving the second reading of the Bill in the House of Lords on March 3. Since some of the existing plant will not be fully operated, and because of obsolescence, the net increase in output capacity in England and Wales will be just over 10 million kilowatts, while the South of Scotland Electricity Board expects to commission more than 1 million kilowatts of new plant and the North of Scotland Hydroelectric Board about 460,000. The load factor is expected to increase to 49·2 per cent by 1964–65, and Lord Mills hoped that substantial improvements could be made in the methods of transmission and distribution so as to reduce the need for overhead lines in the countryside. The Boards had very much in mind the need to find means of diminishing the impact of their lines on amenities. Apart from the hydroelectric plant in the north of Scotland, practically all this new plant would be coal-fired or nuclear, and it was estimated that nuclear power could absorb nearly 47 per cent of the £1,100 million which the Central Electricity Board proposed to spend on power station construction. The nuclear power programme for 1964 onwards had not yet been decided, but apart from water-power we intended to rely in the long-term on coal and on nuclear power: less than 4 per cent of the investment in power stations proposed over the next seven years represented oil-fired plant.

These statements form a background to the third White Paper* on capital investment in the coal, electricity and gas industries, which is limited to the years 1957–59. Actual expenditure in 1957 was £434·7 million, compared with £438·9 million and £524·7 million approved for 1958 and 1959, respectively. Of these figures, £240·2 million, £241·3 million and £303·5 million are for the Electricity Council and Boards in the respective years: actual expenditure in 1958–59 is estimated to have been £258·5 million, of which £106·5 million was for conventional power stations and £38·0 million for nuclear power stations. The corresponding figures in the approved 1959–60 programme are £117·5 million and £57·0 million, and payments in respect of the nuclear power stations at Bradwell, Berkeley and Hinkley Point will reach their peak during the year. The North of Scotland Hydroelectric Board's programme of capital expenditure of £10 million on generation for 1959 is mainly for hydroelectric schemes at present in hand, while that of the South of Scotland Electricity Board of £16·2 million on generation in 1959 is almost entirely accounted for by the nuclear power station at Hunterston and the coal-fired station at Kincardine.

* Capital Investment in the Coal, Electricity and Gas Industries. Pp. 8. (Cmnd. 713.) (London: H.M. Stationery Office, 1959.) 6*d*. net.

BATHYSCAPHE *F.N.R.S.* III

One of the greatest recent advances in methods of deep-sea research is that of direct observation under water by photography, television and the human eye. The latter had already been shown possible before the Second World War by Otis Barton and William Beebe in the cable-dependent bathysphere.

In 1939, Prof. Auguste Piccard and Prof. Max Cosyns gained the support of the Fonds National de la Recherche Scientifique Belge (F.N.R.S.) to build their free-navigating bathyscaphe, but owing to the War its construction was delayed. The first tests were made in December 1948 off Dakar in the vessel which was entitled *F.N.R.S.* II, the Piccard–Cosyns stratosphere balloon being *F.N.R.S.* I. A depth of 1,380 m. was achieved without passengers. Although improvements were needed, the possibilities of the bathyscaphe were proved, and in October 1950 an agreement was signed between the Belgian Fonds National de la Recherche Scientifique, the French Navy, and the French Centre National de la Recherche Scientifique for the construction by the French Navy at Toulon of *F.N.R.S.* III, using the sphere of bathyscaphe *F.N.R.S.* II. This new vessel was put into the water in June 1953 and Capitaine de corvette G. Houot was placed in command with Ingénieur du génie maritime P. Willm to assist. Together they carried out a series of tests ending off Dakar in February 1954 when they reached a depth of 4,050 m.

In May 1954 the French Centre National de la Recherche Scientifique obtained permission from the Navy to equip and use *F.N.R.S.* III for scientific purposes. A management committee was appointed under the stimulating presidency of Prof. Louis Fage. The first dive was made on April 18, 1954, at a position 25 miles south-west of Dakar to a depth of 850 m. with Prof. Th. Monod as the scientist on board; this was quickly followed by a dive to 1,400 m. Thereafter a certain number of dives have been made each year with Commandant Houot on board, accompanied by a qualified naturalist. By the end of 1957, twenty-eight dives had been made to depths between 130 m. and 2,290 m., eighteen of which were deeper than 1,000 m. Eight distinguished and courageous biologists took part. Their names are given here, together with the number of dives each made, because they should be remembered as pioneers of this new era of marine research: Prof. Th. Monod, Dakar (2); Prof. J.-M. Péres, Marseilles (9); J. Picard, Marseilles (4); Prof. Fr. Bernard, Algiers (3); J. Furnestin, Paris (1); Prof. Dubuisson, Liège (1); G. Trégouboff, Villefranche (6); M. Ruivo, Lisbon (1).

Dives were made in the Mediterranean and the Atlantic. *F.N.R.S.* III is equipped with apparatus for recording at any time the depth, temperature and pressure; it has equipment for collecting water samples with contained microplankton; and it has powerful light projectors and automatic cameras. It does not yet possess means for efficient capture of larger planktonic or bottom-living animals, but observations can be supplemented by collections made by the accompanying vessel with pelagic nets and trawls.

A number of individual accounts have already been published, but a general review of the principal results obtained up to the end of 1957 has now been made available*. Since much of the biological information must be obtained by direct observation, it is essential that the accompanying biologist should be experienced, and that he should have a thorough knowledge of the fauna he is to investigate so that he may be able to identify as many organisms as possible. The more dives he makes also the more competent will he become at observing. Given these requirements there is no doubt that the results obtained will be of great value since the depth, temperature and light conditions can be known exactly. Indeed, most interesting information is already forthcoming on the distribution in depth and abundance of some plankton animals. The occurrence of coccolithophores in considerable numbers at great depths has also been established. A noteworthy feature is the abundance of particles in suspension at different depths. It is now known that the subsistence of the bottom sediments is reasonably firm. Numerous small mounds on the sea bottom are common, but prolonged watching has so far revealed no occupants. Unusual habits and movements of deep-sea fish have been observed. The presence of slow currents has been shown by particles drifting along the bottom.

There is no doubt that the value of the bathyscaphe as a tool in marine research has been proved by French scientists, to whom all honour is due; and as a result new models to attempt greater depths are on the way.

F. S. Russell

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* Annales de l'Institut Océanographique fondées par S.A.S. Albert 1er Prince de Monaco. Publiées sous la direction de Louis Fage. Nouvelle Série. Tome 35, Fasc. 4 et dernier: Résultats Scientifiques des Campagnes du Bathyscaphe *F.N.R.S.* III, 1954–1957. Pp. 235–341+planches 17–24. (Paris: Masson et Cie., 1958.) 1,500 francs.

ALFVÉN WAVES IN A GAS DISCHARGE

By D. F. JEPHCOTT*

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In 1942 Alfvén[1,2] predicted the possible existence of magnetohydrodynamic waves, which may be regarded in the simplest case as transverse oscillations of magnetic field lines carrying with them a surrounding inviscid perfectly conducting fluid.

The velocity of propagation is given by:

$$V^2 = \frac{\mu H^2}{4\pi n M}$$

where H = magnetic field intensity; n = number of particles/cm.^{3}; M = mass of particle.

Alfvén's theory strictly applies only to waves in an incompressible fluid, but it can be extended to a compressible fluid (for example, an ionized gas) for the case of waves of small amplitude. A further restriction is that the frequency should be small compared with the ion cyclotron frequency[3].

Previous experimental work has been carried out in liquid conductors[4-6], and standing Alfvén waves have been reported in some gas discharges[7,8].

Our experiments have been carried out using toroidal gas discharges of 10 k.amp., and 200 µsec. duration, in monatomic gases at initial pressures of about 100µ, and with axial (B_z) fields in the range 3–14 k.gauss. Under these conditions, the current density was nearly constant across the area of the torus (except close to the walls) and the discharge sufficiently quiescent for satisfactory signals to be obtained from magnetic probes.

Fig. 1 illustrates the method used for exciting the waves and measuring their velocity.

When the gas current had reached its peak value, the condenser C was discharged via the spark gap S through the exciter conductors A and B, which were close to the outer wall of the torus. The condenser circuit oscillated at 260 kc./s., imposing perpendicular components on the main field, and resulting in torsional oscillations about the circular axis of the torus.

Oscillations of the order of 10 gauss in amplitude were picked up by the magnetic probe 2 and were found to be delayed relative to the signal from probe 1 which recorded the direct exciting field. No oscillations were observed with $B_z = 0$, and the amplitudes always increased with B_z over the working range. Velocities were calculated after a small correction had been made for the measured time-lag of the perturbing field at D ($d = 0$) in the plasma, relative to the direct vacuum field of the conductors.

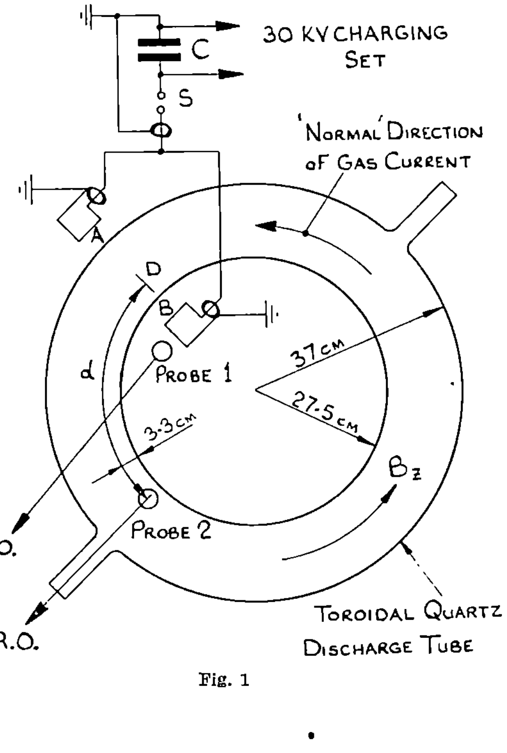

Fig. 1

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* On attachment from Hawker Siddeley Nuclear Power Co.

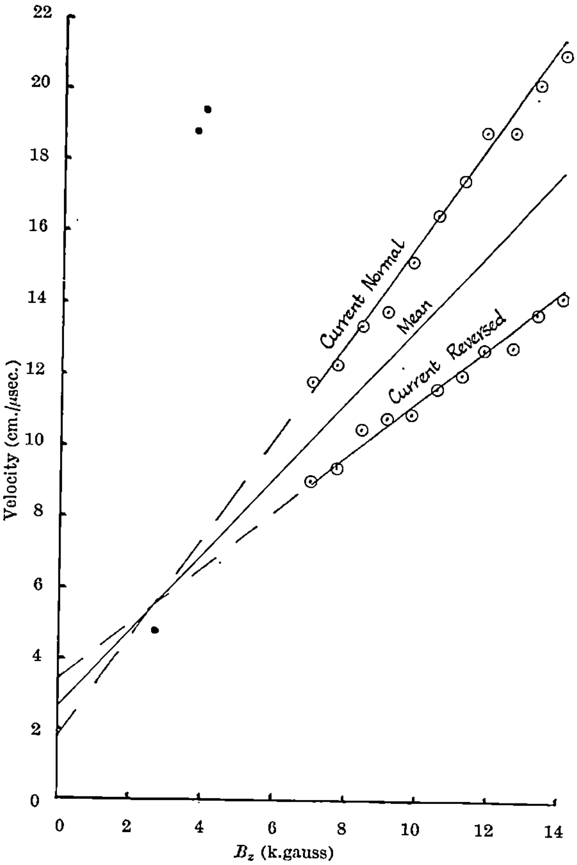

Fig. 2. Argon, 70μ; 10 k.amp.; d = 44 cm.

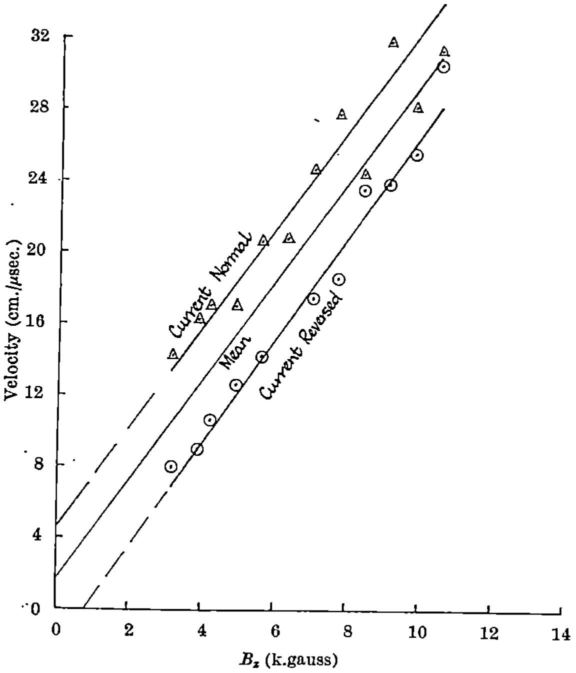

Fig. 3. Helium, 130μ; 10 k.amp.; d = 44 cm.

The velocities have been measured over a range of B_z values, keeping the gas current and initial pressure constant. For argon and xenon, the upper limit to B_z was set by the maximum field available, while in helium the signals became distorted at 10 k.gauss. The lower limit on B_z was set by the value below which the signals were too small to be measured accurately. In xenon, no readable signals were observed with d = 44 cm., and with d = 20 cm. the velocity increased with B_z only for fields greater than 10 k.gauss.

The exciter frequency was well below the ion cyclotron frequency in helium, just below it in argon, and above it in xenon (which probably accounts for the results obtained in xenon).

Velocities were measured with the gas current 'normal' (that is, flowing in the same direction as the waves being propagated from the exciter along the shorter arc to the gas probe) and 'reversed'. In all cases, the measured velocities with gas current normal were found to be higher than with the current reversed, the discrepancy increasing with B_z in the case of argon (see Figs. 2 and 3).

A theoretical treatment[9], involving the interaction of the axial current with the perturbed field, shows that some dependence of the velocity on current direction is to be expected, but at present the numerical agreement with experimental results is correct only in order of magnitude.

For the present, we assume the wave velocity to be given by the mean of the velocities measured with the current normal and current reversed.

The positive intercepts on the velocity axes in Figs. 2 and 3 may be due to two possible causes:

(1) No correction has been made for any increase in wave velocity due to damping.

(2) Since the axial magnetic field along any arc is inversely proportional to the radius of the arc, while d is directly proportional to the radius, waves being propagated close to the outer wall tend to lag behind those near the inner wall. Hence, if there is any coupling between waves travelling along arcs of different radii, the wave velocity may be some mean value of the local Alfvén speeds.

Table 1 gives a summary of the results obtained so far in helium and argon. From the Alfvén velocity expression, the ion density has been calculated as given by the slope of the graph of mean velocity against B_z. For argon, the ion density has also been checked with a Langmuir double probe, and the two values for ion density thus obtained show satisfactory agreement. The double probe signals also indicated no changes in ion density due to the passage of the

Table 1

Gas	Gas current (k.amp.)	B_z range (k.gauss)	Range of Alfvén wave-lengths (cm.)	Ion cyclotron frequency range (kc./s.)	Exciter frequency (kc./s.)	Particle density before discharge (No./cm.^{3})	Ion density from wave velocity (No./cm.^{3})	Ion density from double probe (No./cm.^{3})	Electron temperature from double probe (deg. K.)
Helium	10	3–10·5	40–120	$1·14 \times 10^3$–$4·0 \times 10^3$	260	$4·6 \times 10^{15}$	$1·51 \times 10^{15}$	—	—
Argon	10	7–14	40–70	270–540	260	$2·5 \times 10^{15}$	$1·04 \times 10^{15}$	$1·14 \times 10^{15}$	$4·7 \times 10^4$

wave train, and little dependence of ion density on B_z or on the current direction.

The measured velocity of the waves as a function of B_z in different gases shows agreement with theory (except in the case of xenon at low B_z, where the ion cyclotron frequency is appreciably lower than the wave frequency). Hence, in spite of the preliminary nature of the experimental results, there seems little doubt that the oscillations observed were due to the passage of Alfvén waves.

It may be possible, using Alfvén wave velocity measurements of this kind, to determine the ion density of plasmas in magnetic fields, and from measurements of the damping to find the degree of ionization, the electron temperature or the ion temperature, depending on the dominant dissipative process.

I am indebted to Dr. G. Francis and other members of the Atomic Energy Research Establishment, Harwell staff, with whom I have had useful discussions, and particularly to Dr. R. J. Bickerton, who suggested this work, for his help and advice.

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CANALIZATION OF DEVELOPMENT AND GENETIC ASSIMILATION OF ACQUIRED CHARACTERS

By Prof. C. H. WADDINGTON, C.B.E., F.R.S.
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Genetic Control of the Canalization of Development

In multi-cellular organisms the development of tissues and organs commonly exhibits a balance between flexibility and inflexibility; while a sufficient external stress will cause development to divergence and reach some unusual end-result, there are counteracting tendencies to attain the normal adult condition even in the face of disturbing influences. This condition, which has been referred to as the 'canalization of development'[1], must be regarded as a result of the complex interactions between the numerous gene-controlled processes by which development is brought about. It should therefore be possible to modify the degree of flexibility–inflexibility by selection of appropriate genotypes. There has as yet been little direct evidence on this point, although it has been shown that there is some control by the genotype over the repeatability of development (the inverse of developmental 'noise')[2].

Many mutant phenotypes, in *Drosophila* and other organisms, are notoriously sensitive to environmental influences. Experiments were carried out with, among other phenotypes, that of Bar in *D. melanogaster*. The number of facets in the eye is much reduced, but is larger at low temperatures than at high. The offspring of a number of pair matings were divided into two lots, one of which was grown at 25° C., the other at 18° C. Selection was made by breeding from the families with the smallest differences between the family means at the two temperatures. After only five generations, the difference was reduced from about 100 to around 12 (Table 1). The lowering of the difference has involved both an increase in the size of the eye at the high, and a reduction of its size at the low, temperatures; clearly the selected genotypes are much more inflexible (better canalized) against temperature variations. There was no accompanying change in the 'noisiness' of development, as judged by the differences between the logarithms of facet numbers on the two sides of the individual flies.

Table 1. Bar. Facet Numbers in Females in Unselected Controls, and in three Families resulting from Selection

	No. of families	Average family mean, at 18° C., and S.E.	Average family mean, at 25° C., and S.E.	Difference, family means 18° C. and 25° C.
Unselected	9	156·25±4·81	55·46±0·81	100·80±4·52
Selected 6*a*	8	106·02±1·17	96·52±1·67	14·50±2·29
Selected 6*b*	7	100·76±1·38	95·30±1·70	5·46±1·98
Selected 6*c*	8	111·39±1·72	98·48±2·67	12·92±3·05

Genetic Assimilation of an Adaptive Acquired Character

It has been shown that if a strain of organisms is selected for several generations for increased readiness to become developmentally modified in some specific manner in response to an environmental stress, the later generations may exhibit the modification even in the absence of the stress which was initially required to produce it; and it has been argued that this process of 'genetic assimilation' may play an important part in the evolution of adaptive characters[1]. The experiments which have been described so far have dealt with characters which (*a*) would not be adaptive in Nature, and (*b*) the production of which involved threshold phenomena. Both these limitations have been removed in a recent experiment.

Three strains of *Drosophila melanogaster* (Oregon *K* wild-type, sp^2bs^2 and $al\ b\ c\ sp^2$) were grown on normal medium to which sodium chloride had been added in sufficient quantities to lead to considerable mortality (> 60 per cent) of the larvæ. Thus, stringent natural selection occurred; and by increasing the salt concentration in later generations, the intensity of selection was maintained at a roughly constant level for twenty-one generations. At that stage counted numbers of eggs were set up on media of various salt concentrations, and the unselected stocks from which the experiment had started were tested simultaneously. The percentage of survivors was ascertained on each medium, and measurements were also made of the area of the anal papillæ, since it has been suggested by Gloor and Chen[3] that these organs are concerned with the osmotic regulation of the larva, although their exact function is not well understood.

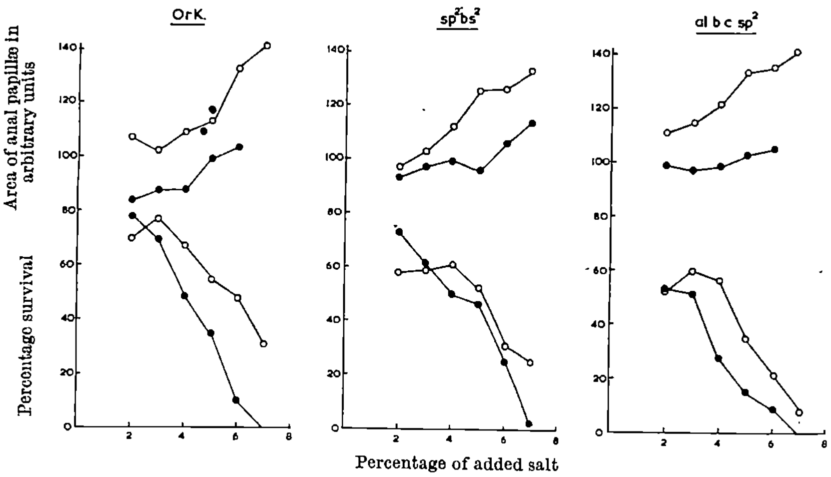

Fig. 1. Percentage survival (below) and size of anal papillæ (above) in selected and unselected strains in various concentrations of salt.

Unselected, ●—●; selected, ○—○

Measurements of the papilla area were made on young prepupæ to minimize alterations due to the contractility of the larva.

As can be seen from the lower graphs in Fig. 1, the selected strains survive better than the unselected at the high salt concentrations, which range up to 7 per cent—twice as high as sea water. From the upper curves, it is clear that the area of the anal papillæ increases in higher salt concentrations. Two points are noticeable: (1) the size of the papilla in the selected strains is greater at all concentrations than in the unselected; (2) the steepness of the curve is increased in the selected strains. The first point indicates that some genetic assimilation has occurred; the selected strains in a relatively normal environment (low salt) have anal papillæ of a size which the unselected strains only attain in response to the stress of added salt. The second point is evidence that the selection has improved the adaptability of the animals, rendering them more responsive to salt concentration. The first point, however, shows that their adaptability is still limited, and it is clearly because of this limitation that some degree of genetic assimilation has occurred.

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CELL GROWTH AND THE DEVELOPMENT OF TUMOURS

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IN the course of biochemical studies[1,2] of liver cell fractions carried out during the induction of liver tumours by known carcinogens, a fairly regular pattern of cell proliferation became apparent. It is the purpose of the present article to relate this pattern to earlier observations by other investigators, and to discuss various implications concerning the carcinogenic process.

In studies in which liver tumours were induced in rats by continuous administration of diets containing 2-acetylaminofluorene[3] or 4-dimethylaminoazobenzene[4], others have shown that grossly recognizable tumours are not obtained until 200 or more days after the animals are placed on the carcinogenic diet. These workers have also shown that it is not necessary that the administration of the carcinogen be continued until tumours are visible; it must be continued only through a certain critical period. For example, if the animals are returned to a normal diet after only 25–30 days exposure to 2-acetylaminofluorene or 4-dimethylaminoazobenzene, few if any will develop tumours; if they are exposed for a total of 50–75 days, a large proportion of the rats will develop tumours, and the number is not greatly increased by continuing the administration beyond this time. This finding suggests two conclusions concerning the neoplastic transformation that ultimately leads to the production of a tumour: (1) malignant cells are not produced unless administration of the carcinogen is continued beyond the time required to produce a significant threshold effect, the nature of which is undefined; (2) when the transformation does occur, it takes place within a relatively short period of time.

In the present experiments, male rats were fed continuously a diet containing 2-acetylaminofluorene. Two such experiments were carried out, using rats of different strains and different initial body-weights (details are given in the legend to Fig. 2). The changes in weights of body and liver obtained in the second experiment are shown in Fig. 1 (the corresponding results in the first experiment were similar). Within a few days of the inception of the carcinogenic treat-

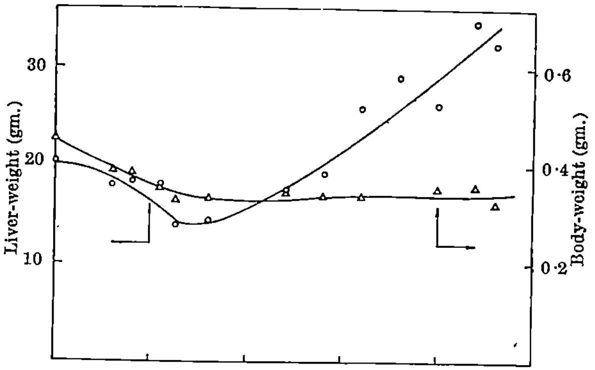

Fig. 1. Changes in weights of liver and body of rats during administration of 2-acetylaminofluorene in the diet, at a concentration of 0·06 per cent

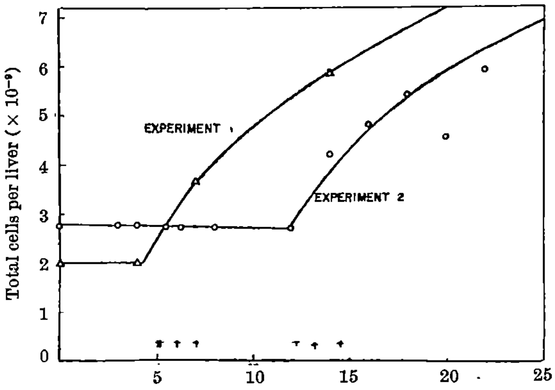

Fig. 2. Changes in the total number of liver cells during administration of 2-acetylaminofluorene, in two different experiments. In Exp. 1, rats of the Holtzman strain, weighing 180–200 gm. at the start of the experiment, were fed a grain diet mixed in the laboratory (ref. 2); the food contained 2-acetylaminofluorene in an initial concentration of 0·05 per cent, which was later reduced to 0·04 per cent. In Exp. 2, rats of the Sprague–Dawley strain, weighing 350–450 gm., were fed a ground 'Purina' diet containing 2-acetylaminofluorene in a concentration of 0·06 per cent. The crosses at the bottom of the graph represent spontaneous deaths of individual rats; the left group of four occurred in Exp. 1, and the right group of three occurred in Exp. 2

ment, the weight of the body fell, until it levelled off at a value distinctly below the initial weight (and even further below the weight of normal controls the weight of which had been increasing in the meantime). In contrast to the fall in weight of the body, that of the liver increased continuously to well above the control values, following a relatively brief initial fall.

The total number of cells in such livers may be determined by introducing appropriate dilutions of a homogenate into a hæmacytometer and counting the cell nuclei present. Since each homogenate is prepared from fresh liver pulp, from which a major part of the connective tissue is removed by use of a tissue press, the cells counted are mainly parenchymal. The changes in the total number of cells per liver are shown in Fig. 2. The course of the changes ran closely parallel in the two experiments. After a period in which no net change in the average number of liver cells was observed, a rapid increase occurred, the rate of which slowed as the carcinogenic period progressed. The increase in number of cells began later in the experiment in which the larger rats were used; the reason for this difference is not understood, but is under investigation. The crosses at the bottom of Fig. 2 represent the spontaneous deaths observed; those on the left occurred in Exp. 1, and those on the right in Exp. 2. It is evident that in each experiment a critical period occurred, at which time some of the animals died and the number of liver cells in the survivors started to increase rapidly. The limitation of spontaneous deaths to the brief period when active cell proliferation was first beginning suggests that a crisis was precipitated by a decrease in the functional capacity of the liver which made a rapid proliferation of liver cells necessary to save the animal from death. The critical period thus defined in physiological terms apparently corresponds in timing to the critical period through which administration of the carcinogen must be continued to obtain a high incidence of animals with tumours.

If such a critical period occurs during carcinogenesis in other organs, it would not necessarily be accompanied by an increase in mortality, if the target organ were one not required for survival, or if destruction were local in the organ (experimental skin carcinogenesis, for example). Survivors who have developed leukæmia since the atom bomb explosions in Hiroshima and Nagasaki quite generally showed signs of severe damage to the blood-forming organs soon after the exposure[5], and, of course, many of the individuals with severe damage of this sort died at that time. Thus development of leukæmia may be similar to hepatic carcinogenesis, to the extent that in both cases a tissue or organ essential to survival is damaged so severely that its total functional capacity is greatly reduced, with the result that some of the victims succumb immediately whereas others enter a period of active repair, characterized by rapid proliferation of the surviving cells in the damaged tissue. In some cases during this period of active proliferation in damaged tissue, malignant cells are produced, the presence of which is revealed only after sufficient time has elapsed to permit their multiplication to produce recognizable tumours.

When instead of 2-acetylaminofluorene, rats were fed 3′-methyl-4-dimethylaminoazobenzene, an azo dye and a well-known hepatic carcinogen, the changes in number of cells shown in Fig. 3 were observed. The time-scale is much expanded compared with Fig. 2, and the curve therefore constitutes essentially a magnification of the early changes seen in the two curves of Fig. 2. Although the carcinogen used in this experiment differs from 2-acetylaminofluorene both chemically and in its pathological effects, it produced very similar changes in the total number of liver cells: an initial period without change in number of cells, followed by an abrupt increase in the number of liver cells. In this case, the number of cells in the liver increased by 50 per cent in two days.

Since the tumour cells occur in discrete nodules which grow separately from the rest of the tissue, and since numerous mitotic figures are found within the tumour mass, it seems likely that growth of the tumour occurs not by continued transformation of liver cells into tumour cells, but rather by proliferation of the tumour cells themselves. It is probable that each discrete tumour arises from one malignant cell. If we consider the actual number of cells involved in the sudden 50 per cent increase noted in the experiment with 3′-methyl-4-dimethylaminoazobenzene described in the preceding paragraph, we find that 10^9 new cells were formed in 48 hr. If this is the case, then to produce 100 tumours, a malignant change would have to occur in only one cell per ten million new cells formed. Even if only 1 per cent of the cells undergoing a malignant transformation

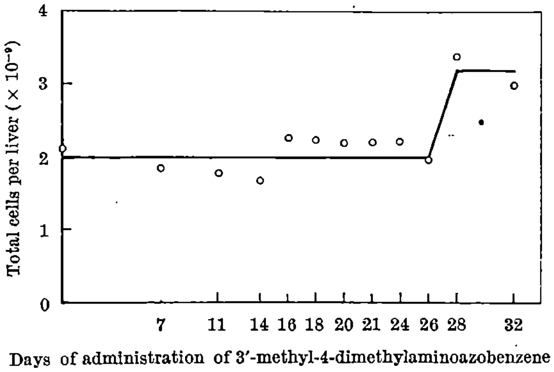

Fig. 3. Changes in the total number of liver cells during administration of 3′-methyl-4-dimethylaminoazobenzene. Note that the time-scale is much expanded compared to Figs. 1 and 2

Table 1

Given : Weight of tumour-bearing livers, approx. 35 gm.
Weight of tumours, approx. 4 gm.
Cell count, per gm. liver, approx. 200 × 10^6
Cell count, per gm. tumour, approx. 450 × 10^6
Then : Tumour-bearing liver contains about 8,000 × 10^6 cells, of which about 1,800 × 10^6 cells are tumour cells and about 6,200 × 10^6 cells are liver cells.

If 4 gm. of tumour constitute :
(1) All one tumour mass, all from one cell : then 31 cell generations would be required.
(2) 4 separate tumours, 1 gm. each, each from one cell : then 29 cell generations would be required.
(3) 4,000 separate tumours, each 1 mgm., each from one cell : then 19 cell generations would be required.

But the liver started with 2,000 × 10^6 cells, and contained 6,200 × 10^6 at the end of the experiment : this would require less than 2 cell generations.

survived to produce a tumour, the incidence of malignant change in the above example would still be only one cell in one hundred thousand. In other words, even during continued exposure of liver cells to a carcinogen, the carcinogenic change is probably a very rare event.

In Table 1 are given the data necessary for calculating approximately the number of cell generations required to produce the tumours observed, and also the number of cell generations occurring in the surrounding liver tissue, assuming that all daughter cells survive in both cases. The figures given for weights of liver and tumour are representative of our findings with 2-acetylaminofluorene. The tumour data have been calculated for three conditions : (1) the tumour tissue occurs in the form of a single tumour mass ; (2) the tumour tissue is found as several 1-gm. tumours ; and (3) the tumour tissue occurs in the form of several thousand 1-mgm. tumours. The condition observed in practice most closely approximates the second case, with tumour nodules ranging in number from less than 10 to about 100. The data in Table 1 show that during the period in which the tumour cells have passed through 20–30 cell generations, the surrounding parenchymal liver tissue has passed through less than two cell generations on the average. Without radioautography, it is difficult to know whether such average increases in cell number are due to a few divisions of many cells, or to many divisions of a few cells. However, if the data of Fig. 3, obtained with 3′-methyl-4-dimethylaminoazobenzene, can be carried over to the experiments with 2-acetylaminofluorene, then the increase in cell number observed early in the experiment is due principally to a few divisions of a large number of liver cells, since the 50 per cent increase in number of cells observed in that experiment occurred within too brief a period of time to permit many cycles of cell division to be repeated. It might be pointed out here that in the very rapid cell multiplication that occurs in liver regenerating after partial hepatectomy, the total increase in number of cells also amounts to less than two cell generations on the average, and since such an increase in cell number is preceded by an increase of more than 50 per cent[6] in the average content of deoxyribonucleic acid per nucleus, it is probable that here, too, the increase in mass of liver is due to a few divisions of many cells.

If at first less than one cell in a million is producing progeny that would eventually yield tumours, then the rapid initial rise in the total number of cells in the livers must be due primarily to multiplication of liver cells rather than potential tumour cells. If this is true, then much of the mitotic activity of the liver cells is already completed soon after the initial burst becomes evident. Comparison with the earlier data[3,4] suggests that this initial burst of cell division is the essential feature of the critical period through which the administration of the carcinogen must be continued in order to obtain a high incidence of animals with tumours. Unless the administration of the carcinogen is maintained until the burst of cell division is produced, few, if any, malignant cells are produced. Once this burst of cell division is elicited, sufficient malignant cells are produced to make further administration of the carcinogen unnecessary. Since the critical period is so short, it is evident that the change from a normal liver cell to a malignant cell can occur within a short time, possibly within one or two cell generations. This suggests that the change essential to malignancy is sudden and complete, rather than continuous over many cell generations. Further important changes in the direction of increasing anaplasia and independence of normal growth-control mechanisms are known to occur[7], but we are considering here only the initial, essential step.

This work was performed under the auspices of the U.S. Atomic Energy Commission.

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GEL FILTRATION: A METHOD FOR DESALTING AND GROUP SEPARATION

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We wish to report a simple and rapid method for the fractionation of water-soluble substances. The method is based on a column procedure similar to chromatography in which the stationary phase is comprised of a new type of gel. These gels consist of hydrophilic chains which are cross-linked. They are devoid of ionic groups, the polar character being almost entirely due to the high content of hydroxyl groups. While water-insoluble, the gels are nevertheless capable of considerable swelling. The fractionation depends primarily on differences in molecular size although phenomena have been observed which indicate the influence of other factors.

The idea that gels might be used for the zone separation of substances differing in molecular size is not a new one. Synge and Tiselius[1], for example, have

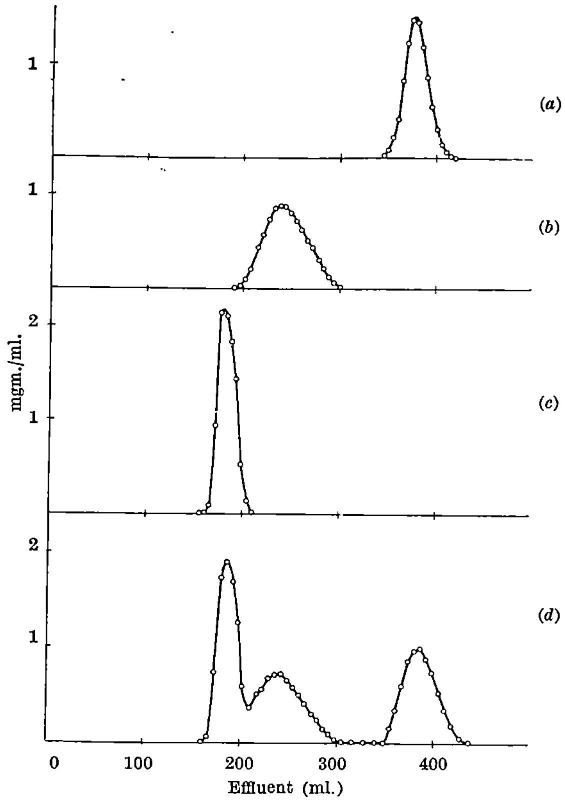

Fig. 1. The diagrams illustrate 'molecular sieving'. In experiments *a*, *b* and *c*, 5 ml. of 1 per cent aqueous solutions of glucose and dextran fractions of $\overline{M}_n$ 1,000 and 20,000, respectively, were filtered through a dextran gel column of the size 4·0 × 36·5 cm. Diagram 1*d* shows the result of a similar experiment with a mixture of the substances mentioned

suggested such a method, based on the effect of friction during electro-osmotic migration through gels. In a homologous series of uncharged substances the friction may be expected to rise with increasing molecular weight. Thus the higher homologues should be retarded more strongly than the lower ones. This is, in fact, the case as was experimentally confirmed by Mould and Synge[2].

On filtration through a bed of starch particles, high and low molecular weight substances also behave differently. In this case, however, it is the lower molecular weight substances which are retarded. We frequently encountered this type of phenomenon when using starch as a supporting medium in zone electrophoresis[3]. It appears likely that the cause of this behaviour is a restricted diffusion of the kind observed by Biget[4]. The restriction is related to the effect of friction observed when solutes are electro-osmotically transported through gels.

Lathe and Ruthven's meticulous and thorough investigation[5] gives a good conception of the possibilities which are inherent in starch filtration. However, starch itself has several undesirable properties. Among these are instability, poorly defined composition and the high resistance to flow of starch columns. Together, these properties have caused the method to be of little practical importance so far.

The above disadvantages seem to be eliminated in the case of certain synthetic gels such as dextran gel. The latter is a material originally synthesized in an attempt to obtain an ideal convection depressor[6] for preparative zone electrophoresis. It is prepared by cross-linking dextran in such a way that the polysaccharide chains form a macromolecular network of great stability. A bed of particulate water-swollen dextran gel has very interesting properties. Aqueous solutions filter rapidly through it at ordinary pressures, and no significant quantity of the gel material is dissolved whether in alkaline, neutral or acid medium. Macromolecules are completely excluded from the gel phase and migrate without retention in the interstitial fluid. However, substances of low or intermediate molecular weight penetrate the gel particles to an extent which is in most cases determined by their molecular dimensions and the degree of cross-linkage of the gel. The separating ability of columns packed with dextran gels is based on these facts.

We have studied dextran gels ('Sephadex' obtained from Pharmacia, Uppsala, Sweden) with varying degrees of cross-linkage graded on the basis of water regain[8], and also other hydrophilic gels derived, for example, from starch and polyvinyl alcohol. Like dextran gels, the latter are chemically stable and as a rule have satisfactory mechanical properties. Moreover their separation properties may be varied within wide limits. More detailed reports will be published later. A few simple examples of the use of the method will be given here.

Some experiments with dextran fractions[7] and glucose are shown in Fig. 1. A glass tube with an inner diameter of 4·0 cm. was packed with 100 gm. of dextran gel suspended in distilled water. The final height of the bed was 36·5 cm. The particle size of the dried form of the gel was between 100 and 200 mesh and its water regain was 2·5 gm. per gm. of dry weight[8]. A filter paper was placed above the flat surface of the bed to prevent disturbances. The test solution was applied and when it had completely entered the bed the column was washed with distilled water at a constant rate of 110 ml./hr. The carbohydrate content was determined using the anthrone method. The recoveries in experiments 1*a*, 1*b*, 1c and 1*d* were 103, 95, 101 and 97 per cent, respectively. The elution volume of the substances and their distribution are independent of whether the substances are filtered through the columns singly or together. The oligosaccharide fraction has a wider distribution than the other substances due to poly-

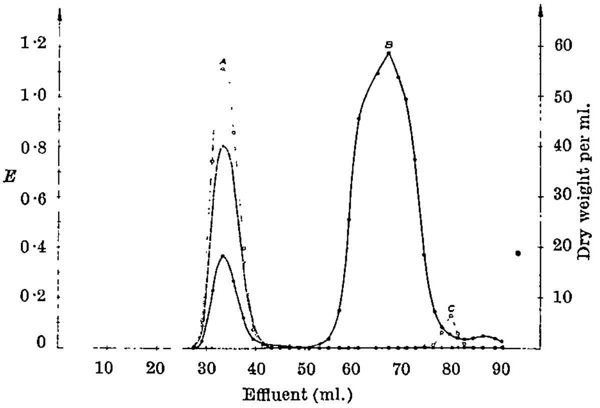

Fig. 2. Diagram showing the separation of ammonium sulphate from serum proteins as obtained after filtration of the solution of the mixture through a dextran gel column (2·5 × 17·5 cm.). Fractions (2 ml. each) were collected and analysed by the method of Folin–Lowry (0·01 ml. aliquots, — × —) and by ultra-violet light absorption at 280 mμ (— ○ —). The weight distribution of the substances in the effluent (— ● —) was determined by weighing 1-ml. aliquots after evaporation *in vacuo*

dispersity. On filtration it is fractionated, and molecular weight determinations of the material from different parts of the peak indicate that the higher homologues are located at the beginning of the peak.

An experiment with serum proteins performed in order to demonstrate desalting is shown in Fig. 2. 5 ml. of a saturated ammonium sulphate solution was added to 5 ml. of fresh human serum and the precipitate was removed by centrifugation. 3 ml. of the supernatant was applied to the top of a bed (2·5 × 17·5 cm.) of the same type of dextran gel as in the previous experiment. The substances were eluted with distilled water at a constant rate of 25 ml./hr. A qualitative analysis for sulphate ions in peak *A* was negative, showing that the proteins had been freed effectively from salt. No proteins could be demonstrated in peak *B*, which contains the entire amount of ammonium sulphate. Peak *C* contains a low molecular weight substance with an absorption maximum at 292 mμ. The yield of material absorbing in ultra-violet at 280 mμ was 102 per cent, that is, it was quantitative within the limits of error.

The result of a gel filtration is often similar to that obtained by dialysis. The unavoidable dilution is naturally a disadvantage but it may be kept within reasonable limits by a suitable choice of experimental conditions. It should be mentioned that the rate of elution and the concentration of solutes can be varied greatly without causing a serious spreading of the zones or altering the position of the peaks. It is necessary in each problem of separation to compromise with respect to those factors which condition the separation efficiency and the rate of elution.

As a desalting method gel filtration presents many advantages relative to dialysis. For example, we have never observed complications corresponding to the clogging of dialysis membranes. The method is especially suited for changing a protein solution from one buffer system to another, a step which is often necessary prior to ion exchange chromatography and electrophoresis.

Gel filtration may be performed with great rapidity and nevertheless causes the complete separation of two or more substances or classes of substances if the differences in molecular size are sufficient. The scale of a procedure such as the desalting of a protein solution may be increased upwards without difficulty so that considerable quantities may be handled.

Since after each complete operation the gel is automatically regenerated, gel filtration is well suited for cyclic purification procedures.

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OCCURRENCE OF 'ESTER-LIKE' LINKAGES IN COLLAGEN

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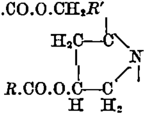
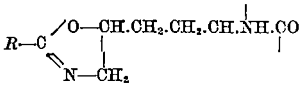
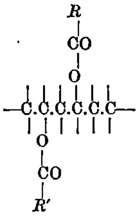
MANY investigators have considered the possibility that primary linkages other than peptide or iminopeptide bonds contribute to the stability of the collagen structure. Thus, Gustavson[1] postulated the existence of ester linkages between the hydroxy groups of the abundant hydroxyamino-acid residues of collagen and the carboxyl groups of terminal residues or of dicarboxylic acid residues elsewhere in the protein. Ames[2] discussed the possible occurrence of an imide cross-linking bond of the *R*.C = O.NH.C = O.*R′* type. In Table 1 are listed some of the primary linkages other than peptide which are possible for collagen. Except for the diester compounds, linkages to carbohydrates have not been included, since the small amount of carbohydrate found in purified collagens could not account for the extent of the hydroxylamine reaction as described here. Except for the side-chain amide and guanidine groups, cleavage of the linkages listed in Table 1 could result in significant decreases in the molecular weight of collagen, and, except for the additional case of interchain peptide bonds, in the production of defined polypeptide units or the separation of individual chains. The presence of acid anhydride bonds to account for the experimental findings is not likely when one considers the conditions under which commercial gelatins are prepared.

It is known that esters may be differentiated from amides or peptides because of their much faster rates of reaction with hydroxylamine at *p*H values of 8–11, and that imides of the type shown in Table 1 may be as reactive as esters. Williams *et al.*[3] showed that certain γ-glutamyl peptides were sensitive to treatment with aqueous hydroxylamine, and Braunitzer[4] claimed that a cyclic iminopeptide linking the β-carboxyl group of an aspartic acid residue and the imino group of a proline residue was cleaved by relatively mild treatment with hydroxylamine. The latter observation led Braunitzer to conclude that an N-terminal proline group of tobacco mosaic virus protein is masked by such a combination, a view which Narita[5] could not confirm.

In the experiments described here, at least three types of gelatin were used: commercial acid- and base-processed gelatins, and gelatins prepared from calf-skin and carp swim-bladder procollagens by mild heating in water or by denaturation with 6 *M* urea. Treatment with hydroxylamine was performed either at room temperature or at 40° C.; in the former case 6 *M* urea was present during the reaction to prevent gelation. Solutions of gelatin containing 2–4 per cent protein were mixed with equal volumes of 2 *M* hydroxylamine hydrochloride solution previously adjusted to *p*H of approximately 10 with sodium hydroxide. In kinetic studies, aliquots were

Table 1. POSSIBLE HYDROXYLAMINE-SENSITIVE BONDS IN COLLAGEN

Type linkage	Structure	Residues which may be involved*
Side-chain amide	$R.CO.NH_2$	$GluNH_2$ or $AspNH_2$
Inter-chain imide	$R.CO.NH.CO.R'$	$GluNH_2$ and Asp or $AspNH_2$ and Glu
Side-chain guanidyl group	$R.NH.C(:NH)NH_2$	Arg
Inter-chain acyl-guanidine link	$R.NH.C(:NH)NH.CO.R'$	Arg and Asp or Arg and Glu
Inter-chain ε-lysyl peptide	$R.CO.NH.CH_2.R'$	Lys and Asp or Lys and Glu
Inter-chain ester	$R.CO.O.CH_2R'$	Ser, Thr or HyLys with Asp/or Glu
Inter-chain ester with HyPro		HyPro with Asp or Glu
Oxazoline from inter-chain ester with hydroxy-lysine		HyLys with Asp or Glu
Inter-chain di-ester with carbohydrate		Carbohydrate with Asp and/or Glu

* The aspartyl and glutamyl residues are conceived of as being linked by means of their β- and γ-carboxyl groups, respectively.

removed at various times and added to 10 *N* hydrochloric acid, bringing them to *p*H 4 in order to stop the reaction. The samples were then dialysed exhaustively against distilled water to remove all free hydroxylamine. Simultaneously with the above reaction, a control mixture of gelatin, containing no hydroxylamine, was maintained at *p*H 10, sampled at intervals, and the aliquots dialysed as above.

The following determinations were then made: protein by a modification of the Kjeldahl method[6] and by the procedure of Lowry *et al.*[7]; N-terminal proline by the method of Piez *et al.*[8], in which terminal proline yields a diminished fraction of the colour given by free proline[9]; amino-groups by the ninhydrin method of Rosen[10]; and amide by the amount of alkali-distillable ammonia produced after hydrolysis with 1 *N* hydrochloric acid for 1 hr. Hydroxamides were measured by three independent spectrophotometric procedures: the classical determination of the magenta complex formed with iron salts such as ferric perchlorate; the quantitation of nitrite produced by oxidation with iodine[11]; and by a method developed in these laboratories, soon to be published, in which hydroxylamine, liberated from hydroxamides by hydrolysis with 1 *N* hydrochloric acid for 3 hr., reacts with indole to yield a coloured product. In addition to these analyses, the protein samples were diluted with equal parts of 1·8 per cent sodium chloride, and studied in a Spinco model *E* analytical ultracentrifuge at 59,780 r.p.m. at 40° C.

With all gelatins studied, the results show that alkaline hydroxylamine causes both a fast and a slow reaction, each characterized by the formation of protein-bound hydroxamide. The fast reaction, which is nearly complete in about 90 min. at 40° C. or in 3 hr. at room temperature, results in a decrease of molecular weight of the protein to a definite end-point of about 20,000. The sedimentation constant changes from the original value of about 3·3 S. for the α-component to a value of about 1·9 S. Fig. 1 shows sedimentation patterns for fish and calf parent gelatins before and after treatment with hydroxylamine, and clearly demonstrates the conversion of both the α- and β-components to the units of lesser molecular weight. During the course of the fast reaction there is no increase in free amino-groups to indicate the splitting of peptide bonds, nor can N-terminal proline be detected. Only late in the course of the fast reaction can one begin to measure a decrease in the number of amide groups; however, when the reaction is allowed to continue beyond this time, a gradual destruction of amide groups and even some cleavage of peptide bonds occur, characteristic of the second or slow phase of hydroxylamine activity.

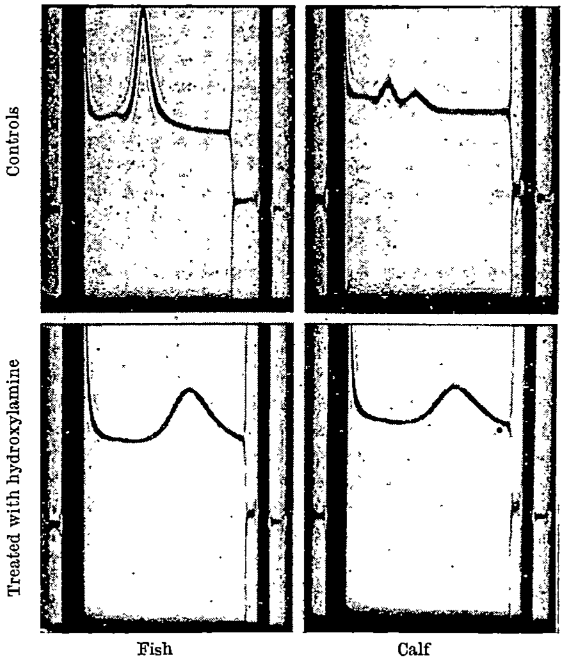


Fig. 1. The sedimentation patterns of parent gelatins obtained from calf and fish procollagens as influenced by treatment with hydroxylamine. The photographs were taken 100 min. after full rotor speed of 59,780 r.p.m. was attained

Only after about 24 hr. at 40° C., however, does treatment with hydroxylamine result in the formation of some dialysable material.

The protein-bound hydroxamide values determined by the methods previously described parallel one another and indicate that about 1 hydroxamide equivalent per 20,000 molecular weight unit is formed during the fast reaction with calf, fish, or acid-processed gelatin. The fast reaction with base-processed gelatin is characterized by the formation of about half this amount of bound hydroxamide, and the slow reaction with this gelatin also shows less hydroxamide production. Such a result is to be expected since ester-like bonds in gelatin could be disrupted by processing with base, and since gelatin produced in this manner contains about 60 per cent less amide nitrogen than does acid-processed gelatin.

We believe that the results summarized above establish the presence of ester-like or perhaps imide linkages between units or chains of about 20,000 molecular weight. It is these units which may be joined together in parent gelatin, or more specifically the α-unit of procollagen, which has a molecular weight of 70,000–80,000. It is of further interest that the components formed by treatment with hydroxylamine retain the capacity to form a gel when used in suitable concentrations of 3 per cent or more.

Grassmann *et al.*[12] and Konno and Altman[13] offered evidence for ester linkages in different collagens using the method of reduction with lithium borohydride. When finely pulverized acid-processed gelatin was suspended in anhydrous tetrahydrofuran containing lithium borohydride, and the mixture refluxed for 30 hr., we could not demonstrate changes in the ultracentrifuge pattern of the protein as compared with a suitable gelatin control; nor did the treated gelatin show a decrease in the amount of hydroxamide formed upon subsequent reaction with alkaline hydroxylamine. Thus it may be concluded that treatment of acid-processed gelatin with lithium borohydride under these conditions does not affect the internal ester-like bonds which are severed when the protein is made to react with hydroxylamine, although it may cause the reduction of terminal ester bonds in native collagens as described by the workers mentioned previously.

An inter-chain acyl shift appears unlikely as an explanation for the action of alkaline hydroxylamine, since the base favours the peptide form. However, in the case of an intra-chain ester-peptide acyl shift involving a residue of hydroxylysine, the ester form may be stabilized by the formation of an oxazoline ring, which, moreover, would probably be sensitive to treatment with hydroxylamine. Should this be the case, it may not be fortuitous that hydroxylysine is present in gelatin in an amount consistent with the bound hydroxamide formed after treatment with hydroxylamine, and this amino-acid might be serving a unique function of cross-linking.

We have begun experiments to separate the components of gelatin after treatment with hydroxylamine, and thus far have isolated two hydroxamide-positive fractions by electrophoresis on paper or starch at *p*H 4·0 in 0·05 *M* acetate buffer. It is our intention to degrade each of the components with bacterial collagenase, and, by suitable analysis, establish the nature of the hydroxylamine-sensitive linkages in gelatin.

Other proteins have been treated with alkaline hydroxylamine for 3 hr. at 40° C., and although several have yielded positive tests for protein-bound hydroxamide, none has formed as much as one-fifth the amount found when equivalent quantities of gelatin are used. Thus crystalline bovine serum albumin, insulin, salmine, and myosin gave detectable hydroxamide reactions, whereas ribonuclease and adrenocorticotrophic hormone did not. Except for albumin, ultra-centrifuge studies were not done, so that it cannot be ruled out that the bound hydroxamide was formed as a result of the splitting of terminal ester bonds or of particularly sensitive amide bonds. Treated albumin, however, showed no diminution of molecular weight as determined in the ultracentrifuge, but rather exhibited a peculiar, and as yet unexplained, aggregation of molecules.

It is also of interest that gelatin, esterified chemically, and afterwards treated with hydroxylamine, showed a large increase in protein-bound hydroxamide as compared with a suitable control.

Gelatins can also be treated with aqueous 1 *M* hydrazine at *p*H 8–9 at 40° C. for 2–5 hr. to cause a cleavage of the protein similar to, though less rapid than, that obtained with hydroxylamine. The products formed are less soluble than the corresponding hydroxamides, but, like the latter, retain a capacity for gelation. They are non-dialysable, and appear to be protein acid hydrazides which can react quantitatively with *p*-dimethylaminobenzaldehyde in acid solution, and which also can reduce copper salts quantitatively. The protein hydrazides can be treated with fluorodinitrobenzene to yield derivatives which are red under mild alkaline conditions (for example, producing red spots on filter paper when exposed to ammonia vapour), and which presumably are dinitrophenyl hydrazides. Both the protein hydrazides and the dinitrophenyl derivatives of these can be digested with collagenase, and the special chromatographic characteristics of the peptides formed are being used at present to establish the precise nature of the bonds cleaved by hydrazine.

In conclusion it may be stated: (1) that various kinds of gelatin are cleaved by either hydroxylamine or hydrazine under conditions favouring the disruption of ester bonds; (2) that these reactions occur without the concomitant splitting of peptide bonds; (3) that the products are non-dialysable proteins of about 20,000 molecular weight which react in one instance as hydroxamides and in the other as acid hydrazides. The results strongly suggest that ester-like bonds exist in parent gelatin, and that the specific disruption of these releases fundamental sub-units of the protein molecule.

This work was aided in part by grants from the National Science Foundation (*G*-4348), the National Institutes of Health, U.S. Public Health Service (*A*-1503), the American Heart Association and the New York Arthritis and Rheumatism Foundation.

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

Corpuscular Radiation and the Acceleration of Artificial Satellites

In a previous communication[1] I showed that the secular accelerations of Satellites 1958 β 2 and 1958 δ 1 varied nearly in unison with the 10·7-cm. radiation from the Sun. This correlation sheds no light on the nature of the radiation responsible for the variations of density of the upper atmosphere, since the 10·7-cm. radiation—the variations of which are remarkably similar to those of the sunspot numbers—can obviously be considered only as a general index of solar activity. To obtain further clues on this subject I reduced anew all the available observations of these two Satellites (about 2,500 for 1958 β 2 and 9,000 for 1958 δ 1) with the best elements at hand and obtained more accurate accelerations at twice the original resolution. The results are plotted in Fig. 1, together with the 10·7-cm. solar radiation curve[2]. As can be seen, the correlation with the solar radiation is remarkably good, even in details, for the high-flying, spherical *Vanguard* Satellite 1958 β 2, for which accurate, well-distributed Minitrack observations were available throughout. For 1958 δ 1 the observations are mostly optical, less accurate and more irregularly distributed, with occasional periods of near-invisibility; this fact, together with the elongated shape, may have contributed somewhat to the poorer correlation in its case.

The procedure for computing the accelerations was as follows. Residuals of individual nodal (for 1958 δ 1) or perigee (for 1958 β 2) passages from empirical equations were plotted and ordinates on the residual curves were read off at intervals of 25 revolutions; differences were taken from the resulting table and accelerations were computed from them. The residual curve for 1958 δ 1 is a succession of long, smooth waves of great amplitude which are mainly due to the 27-day fluctuations. At only two spots in the whole curve is the smooth succession of long waves interrupted by a transient, short-lived but unmistakable secondary oscillation. The dates of these disturbances are July 8–9 and September 4, 1958; they are exactly coincident with the only two great geomagnetic disturbances that occurred during the life-time of the Satellite. Both magnetic storms followed, at the usual 1-day interval, the appearance of a flare of importance 3 on the Sun.

Although the original accelerations had a resolution of 25 revolutions, it appeared possible to obtain significant accelerations with a resolution of 10 revolutions around the critical dates, and these—computed at intervals of 5 revolutions—are plotted in Fig. 2, together with the 3-hr. geomagnetic planetary indices K_p. It is quite evident that in both the July and the September events there was no immediate response at the time when the flare appeared, and that the atmospheric disturbance—an increase in density—proceeded nearly in synchronism with the magnetic disturbance. The increase in the acceleration amounted to 40 per cent in the July 8 event and to a little more than 30 per cent in the event of September 4. These are actually lower limits, since the limited resolution may have smoothed out the peaks (with a resolution of 25 revolutions the peaks are much reduced, as can be seen in Fig. 1, where the two disturbances are marked (1) and (2) respectively). Since the amplitude of the 27-day oscillations did not exceed 20 per cent for this Satellite (1958 δ 1), it appears that the corpuscular radiation capable of causing a first-rate geomagnetic disturbance has a greater, although more transient, effect on the atmospheric density at the 200-km. level than the ordinary

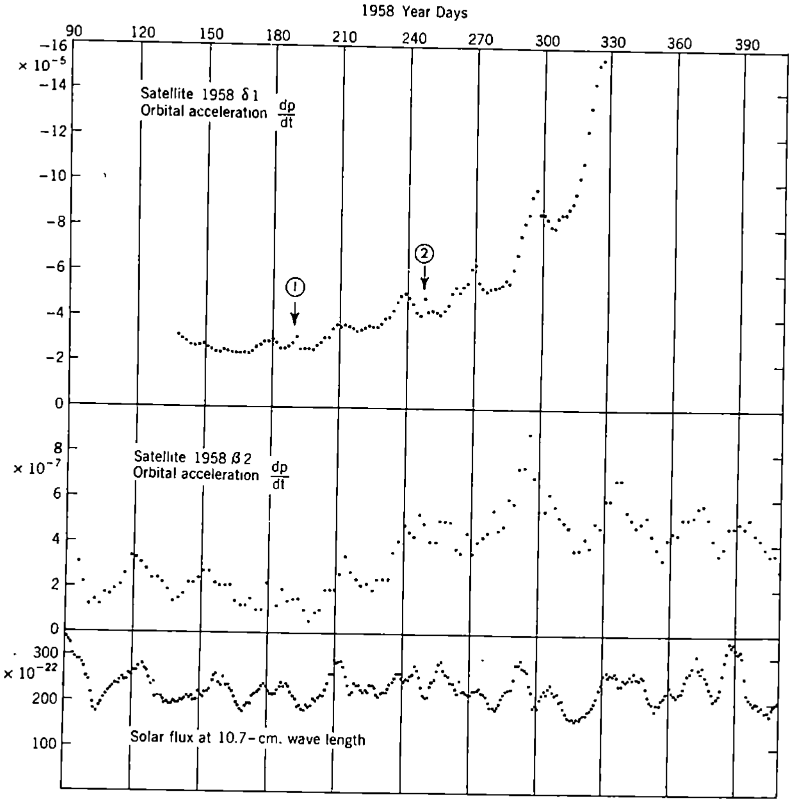

Fig. 1. Secular accelerations of Satellites 1958 δ 1 and 1958 β 2 compared with the 10·7-cm. solar flux. The dates of the two great geomagnetic disturbances, July 8–9 and September 4, 1958, are marked (1) and (2) respectively. Accelerations computed at intervals of 25 revolutions

fluctuation in solar radiation associated with the 27-day period. That this latter radiation is also corpuscular in nature appears quite probable, in view of the failure of the atmospheric density to react promptly to the stream of electromagnetic radiation which accompanies the appearance of a flare.

No disturbance could be detected in the residual curves for 1958 β 2 around the two critical dates in July and September. This may be due to the much smaller value of the acceleration for this Satellite, which would make a short-lived perturbation difficult to detect. It appears quite reasonable, however, that during a violent magnetic storm the atmospheric layers in the 200-km. zone are more strongly affected than those at a height of 600–700 km. If we may judge by the observed increase of the 27-day fluctuations with height[1], it appears that in ordinary conditions the opposite situation prevails, with the higher levels affected more than the lower.

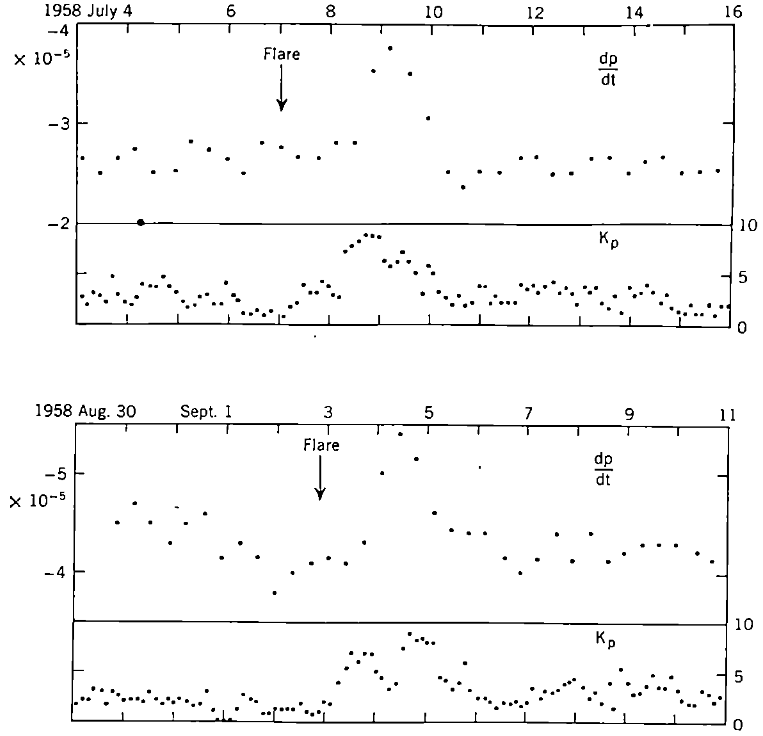

Fig. 2. Secular accelerations of Satellite 1958 δ1 computed with a resolution of 10 revolutions around the dates of two great geomagnetic disturbances and compared with the 3-hr. geomagnetic planetary indices K_p. The instants of the flares that preceded the magnetic storms are marked on the diagram

It might be of interest to remark that at the time of the July disturbance the latitude of perigee of 1958 δ 1 was +35°; at the time of the September disturbance it was +15°.

I am indebted to Mr. Robert Briggs for most of the reductions of the *Vanguard* Satellite observations.

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Massachusetts.
April 30.

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A High-Resolution Survey of the Coma Cluster of Galaxies at 408 Mc./s.

IN December 1958 an area of sky including the Coma cluster of galaxies was surveyed using the 250-ft. radio telescope at Jodrell Bank[1] with a Dicke-type radiometer, pass-band 408 ± 2 Mc./s., and noise figure 6 db. The beam was elliptical, having half-power widths of 40 and 56 minutes of arc. The system was calibrated using the radio source 14*N*5*A*, which was assumed to have a flux of 47×10^{-26} W. m.$^{-2}$ (c./s.)$^{-1}$ (ref. 2). The intensity contours for the region are shown in Fig. 1; Fig. 2 is a sample scan through the cluster and Table 1 gives the fluxes and positions of sources which can be resolved from the extremely complex background.

These results confirm the earlier report by Seeger, Westerhout and Conway[2] that radiation is detectable from the vicinity of the Coma cluster. The new feature of the present survey is the resolution of this radio emission into at least three distinct sources, *A*, *B* and *C* (see Table 1). Of these sources, *A* and *B* are point sources (that is, less than 30 minutes of arc in diameter) since they do not broaden the beam. Source *C* is appreciably extended and could consist of two sources separated by 40 minutes of arc. Although it is apparent from inspection of Fig. 1 that there is a concentration of sources near the centre of the cluster, it is possible that these are not associated with the cluster but are fortuitously coincident with it. The probability of such a coincidence is about 1 in 30. This figure is derived from the number-intensity diagrams given by Mills, Slee and Hill[4] in their survey of radio sources in the southern hemisphere. Thus it is reasonable to assume that some of these sources are physically associated with the cluster.

Current views are that the radio emission from clusters of galaxies may be separated into three components, namely, the normal emission from galaxies[5], the emission from intergalactic gas[6], and emission from abnormal systems. It is important to decide on the relative contributions from these three components for the Coma cluster. Baldwin and Elsmore[7] have shown that in the Perseus cluster

Table 1. FLUXES AND POSITIONS OF SOURCES

Source	R.A.			Dec. N.		Flux (× 10^{-26} W. m.$^{-2}$ (c./s.)$^{-1}$)	Notes
A	12h.	51m.	20s.	27°	57′	6	Probable error of position, ± 5′
B	12	51	20	26	39	2	,, ,,
*C**	12	56	00	28	24	12	,, ,,
D	13	08	10	27	48	6	,, ,,
E	13	16	30	30	10	5	,, ,,
F	12	44	00	26	13	3	,, ,,
G	12	58	00	30	12	2	Probable error of position, ± 10′
H	13	06	30	29	13	1	,, ,,
J	13	12	30	29	11	2	,, ,,
K	13	03	30	24	53	1	,, ,,
L	13	07	00	26	13	1	,, ,,

* Distributed source.

75 per cent of the emission at 80 Mc./s. originates in an abnormal object (*NGC* 1275), which is two galaxies in collision, and the remaining 25 per cent in a much broader component. We have measured the flux from *NGC* 1275 at 408 Mc./s. and find it to be 36 × 10^{-26} W. m.$^{-2}$ (c./s.)$^{-1}$. As the flux of the sources *A*, *B* and *C* is within an order of magnitude of this, they could be peculiar objects within the Coma cluster.

In the presence of these sources, which we shall provisionally assume to be associated with peculiar objects, it is difficult to determine whether a broad component of radio emission exists which is co-extensive with the optical limits of the cluster. If the general background brightness temperature is 2° K., the total emission from the cluster is 26 ± 6 × 10^{-26} W. m.$^{-2}$ (c./s.)$^{-1}$. The total emission from the sources in the cluster is 20 ± 5 × 10^{-26} W. m.$^{-2}$ (c./s.)$^{-1}$. Therefore if a distributed component exists it does not contribute more than 25 per cent to the total emission. This sets an upper limit to the possible contribution from the intergalactic medium and from all the normal galaxies in the cluster.

The outstanding problem is to determine which of the discrete sources are associated with the cluster. For this purpose accurate position measurements are required so that optical identifications can be made.

We thank Prof. A. C. B. Lovell for making available the facilities at Jodrell Bank, and Mr. R. Hanbury Brown for suggestions and criticisms throughout the course of the work. One of us (D. S. M.) gratefully acknowledges a Leverhulme Research Fellowship.

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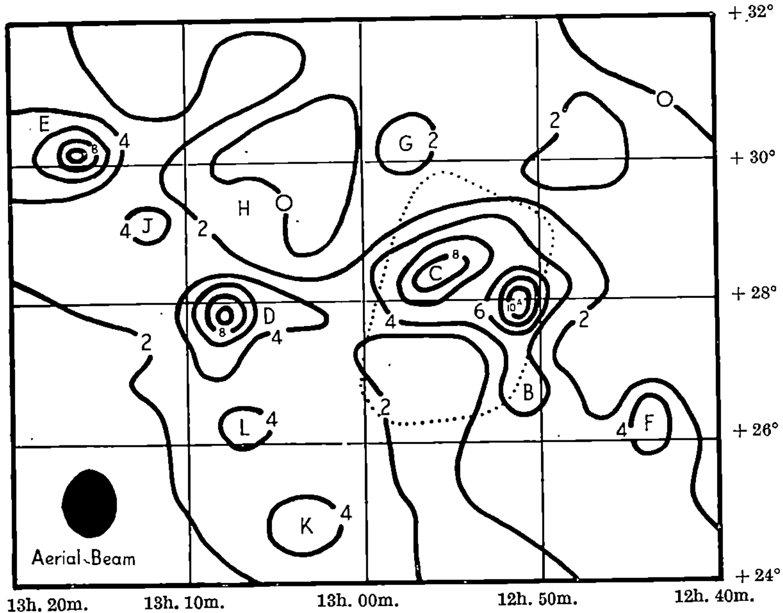

Fig. 1. 408 Mc./s. radio contours of the Coma cluster region (R.A. 12h. 55m., dec. + 28° 20′) plotted in intervals of 2° K. brightness temperature indicating the temperature above a chosen reference region (R.A. 12h. 40m., dec. + 28°). The dotted line is the equal population contour representing 400 galaxies per square degree (ref. 3). The co-ordinates are for epoch 1950.0

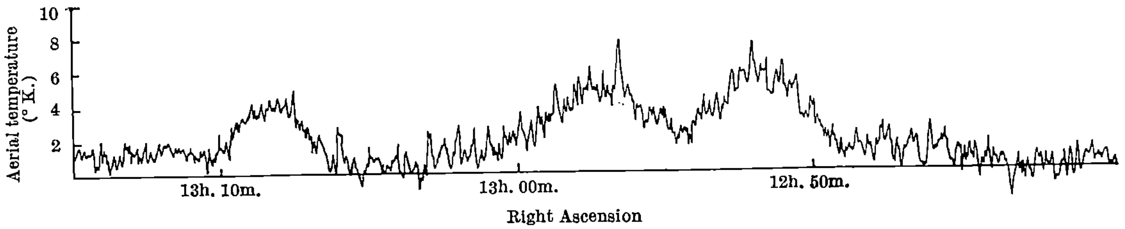

Fig. 2. A typical drift scan through the Coma cluster at declination + 28° 05′

Frequency of Meteorite Falls throughout the Ages

PROF. HANS PETTERSSON has pointed out[1] that the late Prof. F. A. Paneth's statement that "iron and stone meteorites did not fall before the later Quaternary"[2] must be modified since cosmic spherules formed by the ablation of meteorites in the Earth's atmosphere are found in the deepest sections of cores of sediments from the Pacific Ocean dating back to Tertiary times.

There is other evidence which suggests that meteorites have fallen on the Earth's surface at least as far back as the Tertiary. Henderson and Cooke[3] have described the unusual occurrence of the Sardis coarse octahedrite, from which they have concluded that this iron meteorite may have fallen into the middle Miocene sea and become buried by the slowly accumulating middle Miocene 'Hawthorne formation' with which it is now associated. Of even more importance is a previously unpublished report that an iron meteorite was found at a sub-surface depth of 1,525 ft. in an oil well drilled in Zapata County, Texas. The circumstances of the find have been described by M. Williams and forwarded in a personal letter dated September 14, 1956, by E. A. Wendlandt, chief geologist of the Humble Oil and Refining Company.

During the drilling of the well in 1930 an extremely hard object was struck at a depth of 1,525 ft. and in sediments of almost certainly Eocene age. This object was recovered and found to be a piece of metal about the size of a man's fist. An approximate analysis of a 0·4-gm. sample by M. Williams indicated about 82 per cent iron, 5–10 per cent nickel and traces of phosphorus, carbon and silicon. Two surfaces were polished and on etching Widmanstätten figures were quite distinctive. It would seem almost certain that the metal fragment was an octahedrite iron meteorite, but unfortunately the specimen has since been lost. There does not seem to be any reason to doubt the authenticity of the find, and the fact that the meteorite was embedded in Eocene sediments at a considerable depth from the surface could only mean that the meteorite fell in Eocene times.

Recent determinations of 'cosmic-ray ages' of certain meteorites indicate that they were broken from their parent bodies about 10^9 years ago[4]. In these circumstances meteorites have probably been available to fall on the Earth since at least early Palæozoic times. However, most meteorites are unstable on the Earth's strongly oxidizing surface, so that it would be most unlikely that they would be preserved in any readily recognizable form in sediments older than Tertiary. Since cosmic spherules are already largely fused and oxidized, they might be expected to be more stable and perhaps preserved in sediments considerably older than Tertiary.

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Some Experiments with an Electrodeless Discharge

Although various thermonuclear devices such as *Scylla*[1] employ electrodeless discharges to generate strong shock waves in a gas such as deuterium, with the exception of some exploratory experiments of Janes and Patrick[2], there are no reports of attempts to study the basic phenomena in such devices. An investigation of electromagnetically driven shock waves generated by this method is therefore being undertaken at the Atomic Weapons Research Establishment, Foulness.

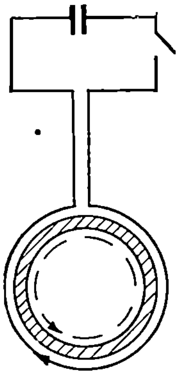

Fig. 1. Diagram of electrodeless apparatus for producing converging shock waves

The apparatus used is shown schematically in Fig. 1. A single-turn coil is wrapped around a 'Perspex' cylinder with 'Perspex' end-walls. The dimensions of the 'pill box' so formed were 3·1 cm. diameter by 2·2 cm. long, and this chamber was filled with deuterium to some known pressure between 0·1 and 2 mm. mercury.

A rapidly rising current was produced in the single-turn coil by suddenly switching an 8 μF. low-inductance condenser bank across it. Under certain conditions of gas pressure, and aided by some pre-ionization, the e.m.f.'s induced in the gas are sufficient to cause breakdown and a cylindrical current sheet is formed in the gas at the circumference of the pill box. This induced current is in the opposite sense to that in the coil, and the repulsion between the two current sheets gives rise to a strong shock wave in the gas.

Streak camera photographs (that is, radius–time curves) of the motion of the shock front showed that the shock did not reach the centre of the pill box. This result is in accordance with the observations of Janes and Patrick[2] and is attributed to some of the magnetic field from the current in the coil penetrating the discharge before the plasma formed by the shocked gas is sufficiently conducting to prevent diffusion of the magnetic field. This weak magnetic field is then trapped and amplified by the imploding shock until the magnetic pressure is sufficient to reduce the shock to rest.

This theory was confirmed by measurements of the magnetic field made with a coil mounted at the axis of the discharge ; these showed a sudden rise as current began to flow in the coil, followed by a period of relatively constant field as the discharge built up and the gas became conducting. There was then an increase in magnetic field corresponding to the implosion of the shock wave. It was, moreover, found possible to make the shock travel much closer to the axis by putting on a d.c. field to cancel out the field trapped by the imploding shock. The degree of convergence is greatly increased by having a d.c. field of the order of 1,000 oersteds. For fields greater than this, the degree of convergence falls again, since the effect has been over-corrected. Also, with fields of the order of 1,000 oersteds, the speed of the imploding shock is increased, presumably because little work is done in compressing the small trapped magnetic field. This may well have important applications to the production of high-temperature plasmas, since the temperature of a shocked gas varies approximately as the square of the shock speed.

The interaction of the imploding shock with the trapped magnetic field is of some interest since it is an addition to the small number of cases where hydromagnetic interactions may be observed on the laboratory scale with magnetic Reynolds numbers in excess of unity. The magnetic Reynolds number may be defined by :

$$R_m = 4\pi\sigma U r_0 \qquad (1)$$

where σ is the conductivity of the plasma (E.M.U.), U is the shock speed (cm./sec.) and r_0 is the radius of the apparatus (cm.).

The physical significance of magnetic Reynolds number is that, in hydromagnetic phenomena, the magnetic lines of force diffuse through the medium or are fixed to conducting particles of the medium if R_m is much less or greater than unity respectively. On the cosmic scale, the linear dimensions r_0 are so large that R_m is normally much greater than unity. On the laboratory scale, however, r_0 is usually limited to the order of ten centimetres, and most attempts to study hydromagnetic phenomena at large R_m have employed highly conducting liquids. The present experiment achieves a high R_m by means of high velocity, U, and fairly high conductivity, σ.

A theory of the variation of trapped magnetic field with shock radius has been formulated and the results presented as a power series in $1/R_m$. The first two terms give a field variation in the form:

$$H \propto \{r(r + \delta)\}^{-(1 - 1/\eta)} \qquad (2)$$

where $\delta = \eta/2\pi\sigma U$, and r is the shock radius (cm.) at time t (sec.), and η is the ratio of densities across the shock front.

This variation has been computed for various shock speeds, the temperature of the shocked gas (and hence σ, ref. 3) being determined from the Rankine – Hugoniot equations taking the ionization and dissociation energies of deuterium into account. The results are presented in Table 1. It will be seen how rapidly the magnetic Reynolds number increases and the distance δ decreases with increasing shock speed.

Table 1

Shock speed (cm./μsec.)	Temperature of shocked gas (° K.)	Conductivity σ (E.M.U.)	Magnetic Reynolds number for apparatus 1-cm. radius	Compression (η)	δ (cm.)
6·0	$5{\cdot}0 \times 10^4$	$2{\cdot}8 \times 10^{-7}$	2·1	7·8	0·74
7·0	$7{\cdot}9 \times 10^4$	$5{\cdot}7 \times 10^{-7}$	5·0	6·3	0·25
8·0	11×10^4	$9{\cdot}3 \times 10^{-7}$	9·3	5·6	0·12
9·0	15×10^4	15×10^{-7}	17	5·3	0·06
10·0	19×10^4	21×10^{-7}	26	5·0	0·04

Equation (2) may be expressed in the form:

$$\frac{1}{H}\frac{dH}{dt} = -U\left(1 - \frac{1}{\eta}\right)\left\{\frac{1}{r} + \frac{1}{r + \delta}\right\} \qquad (3)$$

The values of $\frac{1}{H}\frac{dH}{dt}$ obtained theoretically from this formula have been compared with the values obtained experimentally with the small field-measuring coil. Preliminary measurements indicate that the theory accounts reasonably well for the experimental results.

Another phenomenon that has been observed is that the gas will not break down on the first half-cycle of the oscillatory current in the single-turn coil when the condenser bank is switched across it if the ambient deuterium pressure is below a certain critical value.

An approximate theory of this effect has been derived by postulating that electrons multiply by a Townsend ionization-by-collision mechanism until a certain cut-off time. Providing this time is longer than a certain amount, the gas is sufficiently ionized to become highly conducting and then breaks down with the formation of a shock wave on the first half-cycle. If it is supposed that the cut-off time is determined by a spiralling motion of the electrons in the rising magnetic field due to the current flowing in the single-turn coil, and that when the field has risen above a certain amount the electrons do not travel a sufficient distance in the direction of the induced electric field to have enough energy to ionize by collision, it can be shown that a shock wave is formed on the first half-cycle only if:

$$r_0 V \alpha \gtrsim 6{\cdot}5 \times 10^4 \qquad (4)$$

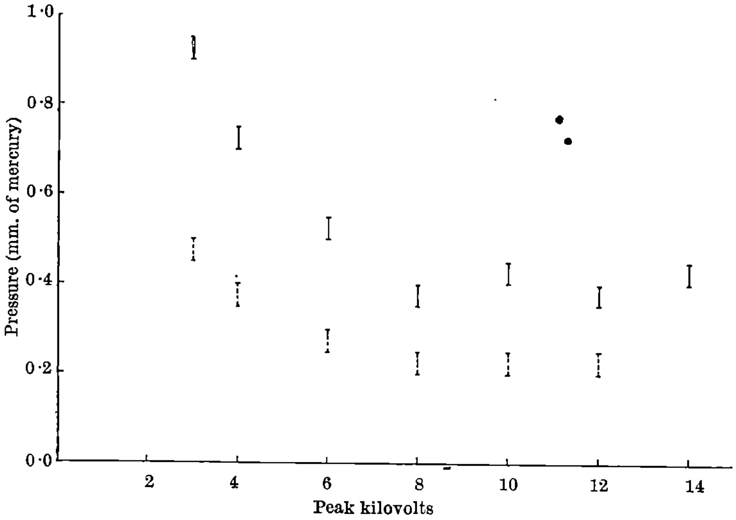

Fig. 2. Minimum breakdown pressure at various voltages for electrodeless discharges of 3·1-cm. diameter (full lines) and 6·2-cm. diameter (broken lines)

where r_0 is the radius of the discharge chamber (cm.), V is the voltage across the coil, α is Townsend's first ionization coefficient.

α is a function of the applied electric field (X in V./cm.) and gas pressure p (in mm.). Experimentally determined values of the minimum pressure at which the first quarter-cycle of the primary voltage produces breakdown are shown in Fig. 2. These values are for two geometrically similar sets of apparatus of different radii. The dependence of the minimum pressure for breakdown on voltage at a given radius is approximately in accord with equation 4, while the predicted dependence on radius for a given voltage is almost exactly fulfilled.

Values of α/p calculated from these curves by means of equation 4 are about twice as large as those determined by Hale[4] and Rose[5]; but in view of the approximations made in the theory, this is considered to be satisfactory agreement.

A full account of the experimental and theoretical work will be published elsewhere. We are indebted to the Director of the Atomic Weapons Research Establishment for permission to publish this communication.

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Use of Synthetic Quartz Crystals as a Support for Specimens in Powder Photographs

In the course of experiments on the hydrothermal growth of quartz crystals from aqueous alkaline solution by the temperature gradient method[1], thin needle-shaped crystals were obtained from the autoclave adhering to the cooler portions of the inside

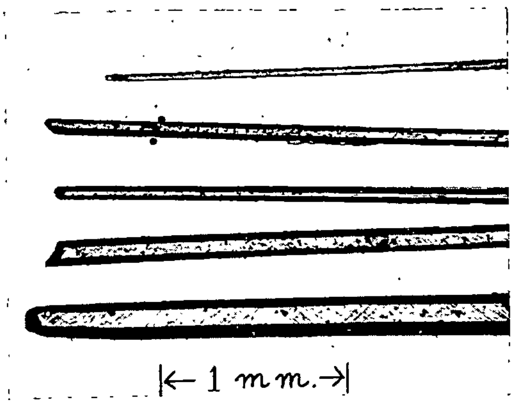

Fig. 1. Examples of needle-shaped synthetic quartz crystals of varying diameters

wall, to the bottom of the lid, and to the stainless steel support for crystal seeds. The autoclave was made of chromium steel, set vertically and heated from below. The solution contained 2 per cent sodium hydroxide and 3 per cent sodium carbonate by weight. The approximate temperature and pressure of the autoclave were 350–360° C. and 300 atm., respectively. The needles were obtained in large numbers pointing almost at random. The diameters of individual needles were uniform and ranged from 0·03 to 0·2 mm. Their lengths were 5 mm. or more. Typical examples are shown in Fig. 1.

The crystals were elongated in the *c*-axis direction with side surfaces bounded by six prism faces and capped at the free end by three uncompleted major rhombohedral faces. Parallel striations usually observed on the prism faces of natural quartz crystal were not observed with the present ones. Each needle was uniform in cross-section and straight in the *c*-axis direction.

The crystal needles serve as excellent supports for powder specimens in the X-ray Debye–Scherrer technique, since they are strong, perfectly stable to air and to X-irradiation, and highly resistant to heat and chemicals. They can be used repeatedly. Powder samples were fixed to the needle with a thin layer of grease. The adjustment making the long axis of the needle coincident with the rotation axis of the specimen holder of the camera could be carried out accurately, since a sufficient length of supporting crystal was straight. The centring of the powder specimen was performed automatically with this adjustment.

Debye–Scherrer photographs taken by this method are shown in Fig. 2. There is no confusion between the patterns of the quartz and the powder, the former appearing as short specks superimposed on the usual Debye–Scherrer pattern. The diameter of the camera was 57·3 mm. The collimator consisted of two pinholes 0·3 mm. in diameter and 51·5 mm. apart. The camera was equipped with a small goniometer head as a specimen mount.

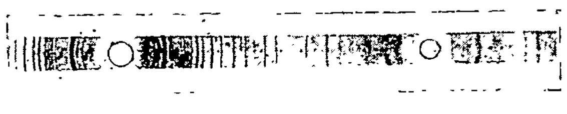

Fig. 2. X-ray powder pattern of germanium and germanium dioxide mixture taken with needle-like synthetic quartz crystal as the specimen support. Radiation, copper $K\alpha$ (filtered)

This method has the following advantages.

(1) The photographs are free from diffuse halos, unavoidable when glass fibres or other amorphous materials are used. This increases the sensitivity for the detection of weak lines.

(2) The equatorial line is easily determined from the rotating crystal pattern of quartz. The centres, $2\theta = 0°$ and $180°$, are easily and accurately obtained.

(3) It gives valuable information on the X-ray spectra giving rise to the powder pattern. Copper $K\beta$, tungsten $L\alpha_1$, or other spectra due to impurities in the target can be recognized by observation of the diffraction spots due to the quartz crystal. The relative intensities of the spectra are also easily obtained.

(4) Departures of the specimen from the correct orientation during exposure is easily detected; the rotation photographs of quartz become similar to 'tilted-crystal' photographs, the diffraction spots becoming longer with the increase in 2θ.

(5) The quartz pattern serves as a good standard for interpolation in the measurement of spacings of the powder pattern. Recently, the variability of lattice constants of quartz crystal by amounts as large as 0·01 per cent has been reported by Keith[2]. Her result shows that the lattice constant, *a*, of synthetic quartz varies from 4·9126 to 4·9131 A., depending on the conditions of its growth. However, for measurements where this amount of variation is negligible synthetic quartz may well serve as a standard.

Measurement of the precise lattice constants of our needle crystals and their variation, if any, under X-irradiation are in progress.

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METALLURGY

Crystallographic Orientation of Nodules formed by the Grain Boundary Reaction of Aluminium–Zinc Alloys

ALTHOUGH the grain boundary reaction phenomenon (discontinuous precipitation or cellular precipitation) of aluminium–zinc alloys was reported previously[1,2], the crystallographic orientations of nodules have not yet been determined. As the spacing between lamellar precipitates in nodules of aluminium–zinc alloys is very small, the precipitates cannot be observed by the ordinary optical microscope, but only by the electron microscope, as shown in Fig. 1. If the precipitates in the nodules are oriented in a definite direction, the relationship of the crystallographic orientations between nodules and matrix grains could be determined[3]. Or, if the specimens can be treated by an adequate etching technique to be sensitive to polarized light, the relationship of the orientations can be observed under the polarized illumination[4]; but this was also impossible for the existence of the small precipitates.

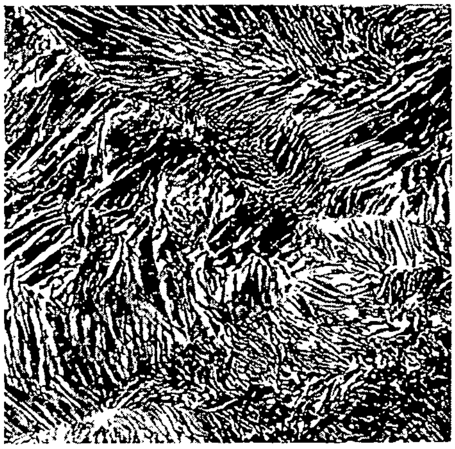

Fig. 1. 25 per cent zinc aged for 250 hr. at 120° C. (× 3,000)

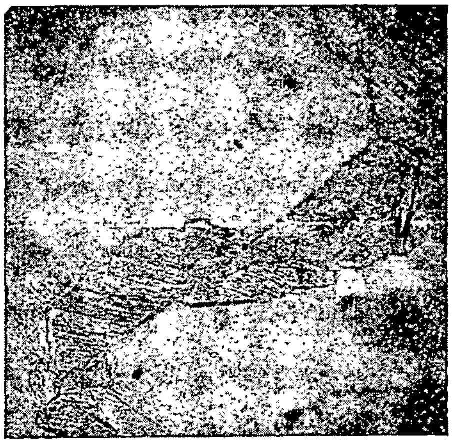

Fig. 2. 25 per cent zinc aged for 600 hr. at 50° C. (× 40)

However, we were able successfully to determine the crystallographic relation by the optical microscope under the polarized illumination after adequate heat treatment and chemical polishing. The technique is as follows. The specimens with nodules produced by ageing, as shown in Fig. 2, are solution heat-treated for a short time, for example about 5 sec., in a salt bath regulated at 470° C. Thus the bulk of precipitates in nodules are dissolved into the matrix and the advancing boundaries of nodules are left as they were. This fact can be observed by means of an optical microscope under polarized illumination after chemical polishing in a solution of 25 parts of sulphuric acid, 70 parts of ortho-phosphoric acid and 5 parts of nitric acid at 135° C., as shown in Fig. 3. In this case, it is most important to keep the temperature of solution at 135° C. exactly, otherwise the specimens are not sensitive to polarized light. The result, clearly shown in Fig. 3, is the same as those obtained in $AlAg_3$, $ZnAg_4$ and $ZnCu_5$ alloys; that is, the crystallographic orientation of a nodule is the same as that of the adjoining grain from which the nodule grew. Moreover, when specimens so treated are aged again, some new nodules are formed at those parts of the advancing boundary which is parallel to the initial grain boundary, but not at the boundary which is normal to the initial one (Fig. 4). This indicates that the growth-rate of nodules depends on the relative orientation of the grain boundaries[6].

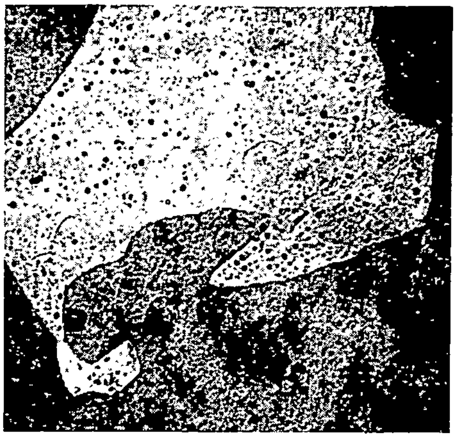

Fig. 3. The same as Fig. 2 except for further heat treatments for 5 sec. at 470° C. (× 40)

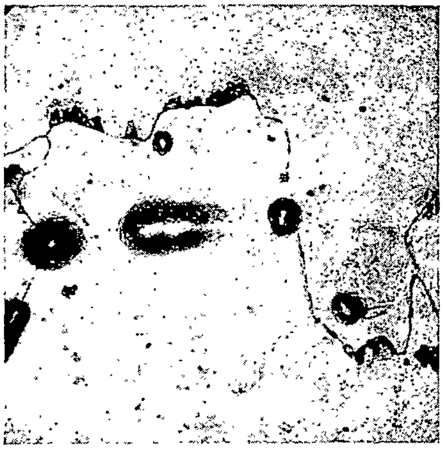

Fig. 4. 25 per cent zinc aged for 10 hr. at 100° C., heat treated for 5 sec. at 470° C. and re-aged for 1½ hr. at 100° C. (× 200)

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CHEMISTRY

Alicyclic Structures in Coals

X-RAY and other physical and chemical evidence indicates that coals assume a graphitic structure with metamorphism. X-ray diffraction patterns of some meta-anthracites show (*hkl*) reflexions that arise from the three-dimensional unit cell of a graphite lattice[1,2]. For the anthracites, a number of diffraction bands

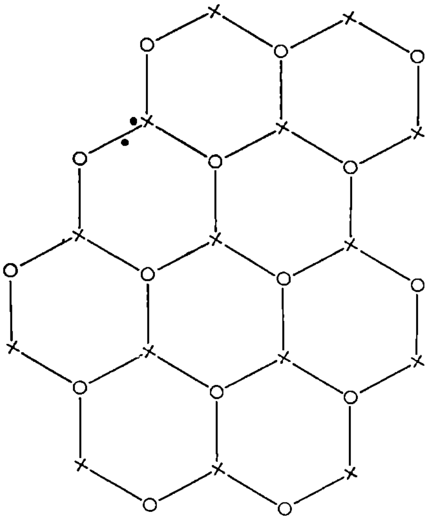

Fig. 1. The molecule used in the calculations. (For the alicyclic case carbon atoms shown as crosses were taken to be in one plane, those as circles in another, that is, a chair configuration)

can be detected which coincide with the (*hk*) reflexions of aromatic layers (having a two-dimensional unit cell of side approximately equal to that of graphite layers)[3]; the remainder of the bands can be attributed to the (00*l*) reflexions of these layers packed 'turbostratically'[4]. Medium- and low-rank coals also give diffuse diffraction patterns that can be indexed as the (*hk*) and (00*l*) reflexions of aromatic layers. These observations led to the development of methods for quantitative analysis of X-ray intensity profiles of coals, permitting estimation of bond-lengths, fraction of carbon in aromatic layers (the remainder assumed to be roentgenamorphous), and size distribution and stacking of the layers[3,5,6].

Coal components rich in hydrogen (more than 6 per cent by weight), for example, exinites[7], resins and some coalified wood[8], show diffraction bands in the angular region where the (*hk*) reflexions of aromatic layers occur. However, the patterns of these components do not have the so-called (002) band. Instead they have a very pronounced peak at smaller angles corresponding to *d*-spacings ranging from 4·3 to 5 A. Despite this ambiguity, exinites were still considered as consisting mainly of condensed aromatic layers, the shift in *d*-spacing being attributed to buckling of the layers or to the presence of more aliphatic material around the edges of the aromatic systems[7].

Treatment of vitrinites with lithium–ethylenediamine results in the addition of considerable hydrogen (as many as 44 hydrogen atoms/100 carbon atoms)[9]. X-ray patterns of treated vitrinites showed extensive changes at moderately low scattering angles[10]. The (002) peak was displaced to lower angles, corresponding to an increase in *d*-spacing from about 3·6 to 4·6 A. Since lithium–ethylenediamine was found to be a powerful hydrogenating agent for aromatic rings without cleavage of C—C bonds[11], the shift of the (002) band to larger *d*-spacings appeared to be consistent with conversion of planar aromatic layers to buckled hydrogenated rings. However, intensity patterns of medium- and high-rank coals treated with lithium–ethylenediamine showed only small changes at high angles, and this seemed incompatible with conversion of aromatic structures to alicyclic or hydroaromatic (partially reduced) structures[9]. Therefore theoretical work on the scattering of alicyclic molecules appeared desirable. Preliminary results of this analysis are presented here, and full details will be published later.

An aromatic molecule containing 30 carbon atoms (Fig. 1) has been chosen as an example. The intensity $J(s)$ in atomic units, scattered at any angle 2θ, was computed by the Debye formula[12]:

$$J(s) = \sum_r \frac{n(r)}{N} \frac{\sin 2\pi rs}{2\pi rs}$$

where $s = 2 \sin \theta/\lambda$, $n(r)$ is the number of interatomic distances of length r within the layer, irrespective of direction, and N is the total number of atoms in the layer. All carbon bonds were taken to be of equal length, 1·4174 A. (cf. ref. 5), and all inter-bond angles to be 120°. After constructing the Patterson function[13] of the molecule and inverting the result by the Debye formula, intensity data were computed numerically on the *Univac* 120. The results are shown in Fig. 2 (dotted line).

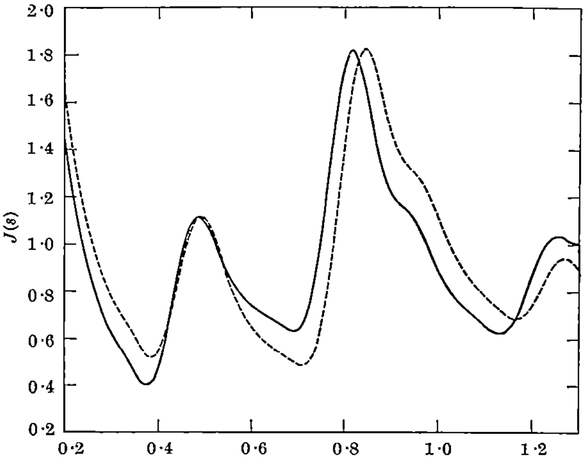

Fig. 2. Calculated X-ray scattering intensities for an aromatic (dotted line) and an alicyclic molecule (solid line) containing 30 carbon atoms (cf. Fig. 1)

A configuration of the alicyclic counterpart of the molecule shown in Fig. 1 was next considered. Carbon atoms shown in the figure as crosses were taken to be in one plane and those as circles in another. All carbon bonds were taken to be 1·5420 A. in length and all inter-bond angles 109° 28·4′, the tetrahedral bond angle. The computed curve is shown in Fig. 2 (solid line).

It is seen that alicyclic molecules give rise to diffraction bands at approximately the same angular region where the (*hk*) reflexions of aromatic molecules occur. The peaks employed for quantitative profile analysis are the (10) and (11) bands of aromatic layers, the first and second peaks from the left, respectively. For the alicyclic molecule shown, the second peak is displaced to a lower angle; however, for other isomeric configurations the displacement is less or even non-existent[14]. It appears that alicyclic or hydroaromatic structure may account to a large extent for the intensity patterns of coal components rich in hydrogen. Indeed, low-rank and even medium-rank coals may contain alicyclic structures in appreciable amounts; diffraction bands of these coals at high angles can be explained by the presence of both alicyclic and aromatic structures. Consequently, it appears that previous quantitative analyses of the X-ray patterns of coal should be re-examined. We wish to thank R. W. Smith for the *Univac* computation.

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Characterization of Molecular Weight Distributions by a Viscometric Method

AN indication of the dispersion of the molecular weight distribution in a given polymer sample may be obtained from values of ratios between the different types of average molecular weight as determined by different experimental techniques[1]. For example, the ratio of weight-average to number-average molecular weights ($\overline{M}_w/\overline{M}_n$) is frequently used for this purpose, $\overline{M}_w$ being obtained from light-scattering and $\overline{M}_n$ from osmotic measurements. The utility of such methods is somewhat restricted because of the uncertainties associated with determinations of the individual molecular weight averages in certain regions of the molecular weight range. Osmometry, in particular, is less accurate for both low and very high molecular weights. Since the percentage error in the derived ratio is approximately the sum of percentage errors of the individual determinations, it is evident that quoted values of $\overline{M}_w/\overline{M}_n$ in the region of 1·05 (typical of a sharp polymer fraction) must be accepted with reserve, because such a figure implies a greater accuracy in the individual methods than their current state of development would appear to warrant. If similar ratios could be obtained by the use of a single technique part of the uncertainty as to the magnitude of possible error would be eliminated. It is the purpose of this communication to propose a method for characterizing the dispersion of a molecular weight distribution based on the measurement of limiting viscosity numbers alone.

The method requires a knowledge of the constants K,a of the Mark–Houwink equation relating the limiting viscosity number $[\eta]$ to the molecular weight M of monodisperse polymer:

$$[\eta]_A = K_A M^{a_A} \qquad (1)$$

$$[\eta]_B = K_B M^{a_B} \qquad (2)$$

Here the subscripts A and B refer to different solvent systems, A being a good solvent and B a poor solvent for the polymer, such that $a_A > a_B$ [1]. The viscosity-average molecular weight $\overline{M}_v$ of polydisperse polymer is then defined by:

$$[\eta]_A \text{ (polydisperse)} = K_A \overline{M}_{vA}{}^{a_A} \qquad (3)$$

$$[\eta]_B \text{ (polydisperse)} = K_B \overline{M}_{vB}{}^{a_B} \qquad (4)$$

It can also be shown[1,2] that:

$$\overline{M}_v{}^a = M_0{}^a \sum_1^\infty w_r r^a \qquad (5)$$

in which w_r is the weight fraction of species of chain length r and molecular weight rM_0. Thus:

$$\frac{\overline{M}_{vA}}{\overline{M}_{vB}} = \frac{\left[\sum_1^\infty w_r r^{a_A}\right]^{1/a_A}}{\left[\sum_1^\infty w_r r^{a_B}\right]^{1/a_B}} \qquad (6)$$

from which it may be shown, using Hölder's inequality, that:

$$\overline{M}_{vA} > \overline{M}_{vB}, \text{ if } a_A > a_B \qquad (7)$$

It follows that the ratio $\overline{M}_{vA}/\overline{M}_{vB}$, which is a function only of a_A, a_B and the molecular weight distribution of the polymer, may serve as an indication of the degree of polydispersity.

In order to illustrate the application of the method to particular cases it is convenient to use the generalized exponential distribution[3,4]:

$$w_r \, dr = \frac{r^z \lambda^{z+1} \exp(-\lambda r)}{\Gamma(z+1)} dr \qquad (8)$$

where

$$\lambda = z/\bar{r} = (z+1)/\bar{r}_w \qquad (9)$$

and in which $\bar{r}$, $\bar{r}_w$ are the number- and weight-average chain-lengths respectively. z is a number which characterizes the type of distribution. Thus $z = 1$ corresponds to the so-called 'most probable' distribution, $z = 2$ to the distribution for low-conversion vinyl polymerizations in which termination occurs exclusively by combination of radicals[3], and increasingly larger values of z correspond to increasingly sharper distributions such as may be expected for fractionated polymer. For this generalized distribution it can be easily shown that:

$$\frac{\overline{M}_{vA}}{\overline{M}_v} = \left[\frac{\Gamma(z+1+a_A)}{\Gamma(z+1)}\right]^{1/a_A} \left[\frac{\Gamma(z+1)}{\Gamma(z+1+a_B)}\right]^{1/a_B} \qquad (10)$$

Values of this ratio are given in Table 1, together with the corresponding ratios, $\bar{r}_w/\bar{r}$, for various values of z, and for values of a_A of 0·80, 0·70, 0·60, assuming a_B to be equal to 0·50 (as in a theta-solvent).

The differences between the ratios $\overline{M}_{vA}/\overline{M}_{vB}$ for different distributions, although small, are suffi-

Table 1

z	$\bar{r}_w/\bar{r}$	$\overline{M}_{vA}/\overline{M}_{vB}$		
		$a_A = 0.80$ $a_B = 0.50$	$a_A = 0.70$ $a_B = 0.50$	$a_A = 0.60$ $a_B = 0.50$
1	2	1·080	1·053	1·027
2	1·5	1·052	1·035	1·017
5	1·2	1·026	1·017	1·009
10	1·1	1·014	1·009	1·005
20	1·05	1·007	1·005	1·002

ciently large to be detectable by simple viscometric methods in current use. These methods are capable of giving viscosity-average molecular weights to an accuracy of at least 1 per cent. Moreover, Hermans and Kooy[5] have described apparatus with which limiting viscosity numbers may be determined with a precision of better than 0·1 per cent. The proposed method is therefore directly applicable within the limits of precision at present attainable, and has the advantage of requiring only one technique of measurement. In addition, measurements of $\overline{M}_{vA}/\overline{M}_{vB}$ may be made comparatively quickly and only small quantities of polymer are necessary. The accuracy of the method will be affected less by errors in the absolute values of the constants of the Houwink equations for the two solvents than by errors in their relative magnitudes. Since values of these constants in different solvents are often obtained by viscometric determinations on the same polymer samples, little error should arise when constants derived in this way are used.

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Direct Examination of the Degradation of High Polymers by Gas Chromatography

Examination of the degradation products of high polymers may give an indication of the mechanism of breakdown, and may also yield information about the structure and composition of polymers and copolymers. Such an examination may be quickly and conveniently effected if the degradation products are characterized by gas chromatography as they are formed. This may be achieved by generating a pulse of degradation products in the chromatographic apparatus, which is so designed that the products are swept into the column with the minimum delay and disturbance.

Two degradation techniques have been applied in this way. In the first method, a few milligrams of polymer sample are used as a dielectric which is broken down by triggering through it a high-energy discharge (up to 2,000 joules). This method has been applied to polyethylene, polyvinyl alcohol, polyvinyl acetate, polyvinyl chloride, polymethyl methacrylate, polystyrene and cellulose acetate. In all cases the degradation is very drastic, the principal products being small unsaturated molecules with acetylene in largest yield. In some cases (for example, polystyrene), 'characteristic' fragments (for example, toluene, styrene, α-methyl styrene) are also obtained; but the yield of these in comparison with the small unsaturated molecules cannot be significantly increased by variation of the experimental parameters. Hence this method is of only limited utility for structure determination, and the secondary thermal effects are so predominant that no information about the mechanism of the primary electrical breakdown is derived.

The second technique may be controlled to give any desired degree of thermal degradation, and has proved to be more versatile in application. The method involves coating or placing the polymer sample on a filament, which can quickly be brought to any specified temperature for a brief period. The temperature calibration of the filament is effected by optical pyrometry and also by melting-point observations. Samples up to several milligrams have been examined, and the sensitivity of the gas chromatography apparatus is such that less than 1 μgm. of a component in the degradation products may be detected.

Two principal applications of this second degradative technique are under investigation. The first is in the rapid estimation of copolymer composition. The procedure here is simply to degrade the copolymer sample at a particular temperature and to measure peaks on the chromatogram characteristic of each constituent of the copolymer; for example, for vinyl chloride – vinyl acetate copolymers the hydrogen chloride and acetic acid peaks have been used. Separate experiments on weighed samples of the pure homopolymers have yielded direct relations between their masses and the sizes of the characteristic peaks, and these relations enable the sizes of the peaks in the copolymer chromatogram to be translated into masses of the two monomers present. In Table 1 the results obtained for three vinyl chloride – vinyl acetate copolymers are compared with those obtained by infra-red analysis.

Table 1. PERCENTAGE VINYL ACETATE IN VINYL CHLORIDE – VINYL ACETATE COPOLYMERS

By infra-red analysis	By degradation
26·7 ± 1·0	26·2 ± 0·8
34·6 ± 1·0	31·4 ± 0·7
44·3 ± 1·0	43·9 ± 0·5

The second application of the technique consists of recording the degradation products from the same sample of polymer maintained for a few seconds at each of a series of temperatures up to 1,000° C. Polystyrene, polyvinyl chloride, polyvinyl acetate and polymethyl methacrylate have been examined in this way, and each polymer gives a characteristic 'spectrum'. (Under the conditions used, the whole temperature-range can be covered in less than half an hour, and the results give a rapid identification of unknown polymers.) The relative proportions of the degradation products at each temperature yield information about the relative importance of the various degradation processes throughout the temperature-range. For example, it can be shown in the case of polyvinyl acetate that simple depolymerization is a relatively insignificant process; that loss of acetic acid is the principal degradation process and occurs at intermediate temperatures, and that the resulting polyacetylene skeleton is much more stable and is degraded principally at the highest temperatures.

This procedure is also being applied to copolymer samples, and a method of distinguishing block from random copolymers is projected.

Full details of this work and of the modifications in hand will shortly be published elsewhere.

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Bond Energies of Some Alkali Fluorides

THE attenuation of microwaves by flames containing traces of alkali metals may be used to determine the electron concentration, arising from the ionization of the alkali, in these flames[1,2]. If a halogen is added to such a flame, the electron concentration is reduced directly by the formation of negative ions, and indirectly by the formation of the alkali halide[3,4]. Flame photometric studies show that the halogens also reduce the excess hydrogen atom concentration in the flame[5]; but it has been observed that fluorine has the least effect[6]. This reduction makes it difficult to estimate the bond energies of the alkali halides from microwave studies[7], because of the indirect nature of the arguments used in the estimations[8]. In the case of fluorine, however, the argument is simplified by the unimportance of the negative ion effect, since the electron affinity of fluorine is low relative to the bond energies of the alkali fluorides, and by the much smaller disturbance produced in the hydrogen atom concentration. In addition, the observations are made at high temperatures where the hydrogen atom concentration approaches equilibrium[5] and it is possible to obtain reliable and consistent results, which it is of interest to place on record.

Sodium fluoride has been examined over the temperature-range 2,300–2,600° K., using perfluoromethyl*cyclo*hexane as source of fluorine, and the dissociation constant determined, assuming the dissociation energy of hydrogen fluoride[9] to be 134 kcal. A graphical determination of the dissociation energy (Fig. 1) gives a value of 124 kcal., equivalent to 119 kcal. at 0° K., in agreement with a statistical 'Third law' value of 120 kcal., calculated from the measurement at 2,400° K. It is also possible to estimate the difference between the bond energies of hydrogen fluoride and sodium fluoride directly from the experimental results. This difference is 14 kcal., which indicates that the bond energy of sodium fluoride is 120 kcal. This concordance shows that the disturbing effects described above are, indeed, negligible. Potassium fluoride could not conveniently be examined over this temperature-range; but a statistical calculation at 2,400° K. gave the bond energy as 117 kcal. Lithium fluoride could only be examined at the highest temperature (2,600° K.) and a statistical calculation put the bond energy at 141 kcal. These values are in good agreement with the thermodynamic predictions of Smith and Sugden[10] but differ somewhat from other authorities[11,12]. They are, however, in good agreement with some values determined by flame photometry in these laboratories recently[13].

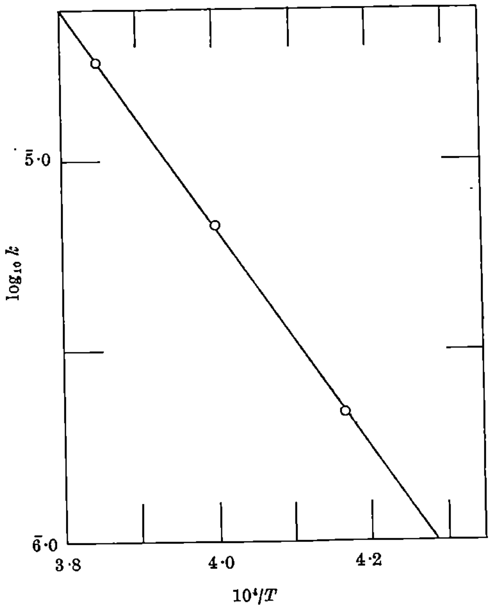

Fig. 1

Thanks are due to Imperial Chemical Industries, Ltd., General Chemicals Division, for the gift of chemicals.

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Tetrahedral Co-ordination in Ni(II)

LINGAFELTER[1] has suggested that the occurrence of blue-coloured $\text{Ni en}_2(NCS)_2$ and $\text{Ni en}(H_2O)_4(NO_3)_2$ for which X-ray evidence gives 6 co-ordination for the nickel atom contradicts the criteria for identifying tetrahedrally co-ordinated Ni(II) suggested in my earlier communication of the same title[2], with the implication that these criteria are invalid.

The basic criterion laid down[2] was the disappearance of the characteristic peak in the region of 400 mμ of octahedrally co-ordinated Ni(II), which usually has a green colour. With the disappearance of this peak, a deep blue colour would be expected to result, other things being equal. A property which would suggest the possibility of a tetrahedral 4 co-ordinate condition would therefore be possession of a blue colour. However, since a shift of the 400-mμ peak to slightly lower wave-lengths could give the same effect so far as the eye alone is concerned, verification by spectral analysis would be an obvious requirement.

Ballhausen[3] has used the absorption spectra of the various stages of complexing of Ni(II) with ethylene diamine to show the spectra of $[\text{Ni en}(H_2O)_4]^{++}$ and $[\text{Ni en}_2(H_2O)_2]^{++}$, and in fact the 400 mμ peak (as well as the others) has been shifted towards lower wave-lengths, but increased, not diminished, in intensity. Dr. R. G. Wilkins, of the University of Sheffield, has kindly shown me a solid preparation of the salt, $[\text{Ni en}(H_2O)_4](NO_3)_2$, which is light blue, and the absorption spectra he has obtained for ice-cold aqueous solutions of the salt correspond closely to that given by Ballhausen[3]. This blue-coloured complex cation therefore meets the criteria for 6 co-ordination of Ni(II), and it is no surprise that X-ray investigation of the related salts verifies this.

My first statement of the mode of identification[2] therefore still stands.

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It would appear quite possible that the disappearance of the 400-mμ peak is indicative of tetrahedral co-ordination of nickel(II), and I have no argument with this criterion. My communication was prompted by Katzin's apparent conclusion concerning the configuration of the blue compounds studied by Lifshitz, Bos and Dijkema on the basis of visual colour alone.

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A Colour Reaction for Thiosulphinates

Investigations of the chemistry of the thiolsulphinates, both synthetic and of natural provenance, would be aided if a rapid colorimetric test for these compounds were available. Aliphatic thiolsulphinates can be characterized, in part at least, by reaction with thiamine[1] or with cysteine[2] to yield crystalline derivatives; but these methods do not generally distinguish thiolsulphinates from thiolsulphonates, since the latter compounds will also react with these reagents. The addition of sodium nitroprusside[3] solution followed by base will yield orange to red colours in the presence of aliphatic thiolsulphinates or thiolsulphonates. This procedure has found application in paper chromatography[3] in investigations of the formation of thiolsulphinates in plants of the genus *Allium*. In our experience, the colour, however, is very fugitive and is apparently not produced by some aromatic thiolsulphinates.

We have found that addition of a solution of N-ethylmaleimide in *iso*propyl alcohol followed by potassium hydroxide in the same solvent to thiolsulphinates yields pink to red colours. Thiolsulphinates can therefore be distinguished from disulphides, which remain colourless. This is an extension of the colour test for thiols reported by Benesch and Benesch *et al.*[4]. The conditions for the test are essentially the same as described for thiols by these authors. The maleimide derivative and potassium hydroxide are used in dry *iso*propyl alcohol solutions, 0·05 *M* and 0·25 *M*, respectively, and the N-ethyl maleimide is used in a very large molar excess over the thiolsulphinate. The reaction may be applied on paper, in which case the paper containing a thiolsulphinate spot is first dipped in the N-ethyl maleimide solution; dried for 5–10 min., and is then dipped in the potassium hydroxide solution. A pink spot develops immediately where thiolsulphinate is present. The test may also be performed in solution in colorimeter tubes and absorbance or per cent transmittance measured.

For colorimetric analysis, 1 ml. of 0·05 *M* N-ethyl maleimide reagent is added to 0·5–5 μmoles of thiolsulphinate in 1 ml. of *iso*propyl alcohol and then 1 ml. of 0·25 *M* potassium hydroxide solution is immediately added. Intensity of colour is conveniently measured at 5150 A. (absorption maximum 5100 A.). The colour fades rapidly during the first 3 min. and then diminishes at a slower rate. Moderately reproducible results are obtained if the absorbance is measured at a specified time between 10 and 18 min. after the addition of alkali and compared with standard curves obtained from measurements of pure compounds. The intensity of colour varies somewhat with different thiolsulphinates. The reaction has been applied to several synthetic thiolsulphinates ($RS(O)SR$) where R is phenyl, *p*-tolyl, ethyl, *n*-propyl, and 2-propenyl. The purity of these compounds was established by infra-red analysis. An allicin isolate from garlic and a low-temperature vacuum distillate from a fresh onion concentrate (both of which were shown to be free of thiols) responded to the test. The reaction is sufficiently sensitive just to detect 5×10^{-2} μmole thiolsulphinate/ml. of solution.

In certain cases, the reaction will distinguish thiolsulphinates ($RS(O)SR$) not only from disulphides but also from thiolsulphonates (RSO_2SR). For example, *p*-tolyl *p*-toluene thiolsulphonate and phenyl benzene thiolsulphonate give no appreciable colour (indistinguishable from the background due to the reagents). Ethyl ethane thiolsulphonate produces a very faint colour, approximately 2 per cent of the intensity of the colour of the corresponding thiolsulphinate and *n*-propyl-*n*-propane thiolsulphonate gives a colour approximately 14 per cent as intense as that of the propyl thiolsulphinate. On the other hand, the colour produced by methyl methane thiolsulphonate is a third as strong as that of ethyl ethane thiolsulphinate (the corresponding methyl derivative was not available for comparison), although the compound was shown to be free of thiolsulphinate by infra-red analysis. The relatively high colour value given by the propyl thiolsulphonate compared with the corresponding ethyl compound may be a result of small amounts of thiolsulphinate as impurity in the former. Other classes of compounds responding to the test are thiols and thiolesters as shown by Benesch and Benesch *et al.*[4], and S-alkyl *iso*thiouronium bromides and aromatic sulphinic acids. In the spectrophotometric method for determining thiols[5] with N-ethylmaleimide in phosphate buffer, the thiol adds to the double bond of the maleimide as measured by the decrease in absorbance at 3000 A. In *iso*propyl alcohol, however, no addition is observed with aliphatic thiols or thiolsulphinates. Whether the addition of base produces a rapid addition to the double bond followed by other colour-forming reactions or whether the reactions follow a different course is not known.

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BIOCHEMISTRY

Direct Determination of Drug Concentrations in Biological Fluids by Polarography

IT is an established fact that part of the initial testing of new drugs involves their estimation in biological fluids from animals or patients receiving the drug. This information is required to establish dosage regimes and to study rates and methods of elimination from the body. Hitherto, the use of physico-chemical techniques such as spectrophotometry, colorimetry and polarography has frequently required a separation of the drug from interfering materials present in the biological fluid. This communication suggests that, in suitable circumstances, the polarographic method can be successfully employed without any such separation.

During the clinical testing of the new anti-tubercular drug 2-ethyl-4-thiocarbamidopyridine (1314 *TH*) it became necessary to determine small concentrations (0·1–5·0 μgm./ml.) of the drug in serum and cerebrospinal fluid, and larger concentrations (>30 μgm./ml.) in urine from patients receiving the drug. Since 1314 *TH* gives a well-defined polarographic wave ($E_{1/2} = -0{\cdot}78$ volt vs. standard calomel electrode at *p*H 7·0) the utility of the polarographic method was investigated. (Full details of the electrochemistry of polarographic reduction of 1314 *TH* and of the methods described below for estimating its concentration in biological fluids will be the subject of further publications.)

It was found that, using a laboratory-constructed, pen-recording polarograph at its maximum sensitivity of 200 mm./μamp., de-gassed, normal sera of the rat, rabbit, horse and human were free from detectable polarographic waves over the potential range −0·1 to about −1·1 volts, using an internal silver wire anode. This potential range is conveniently referred to as the accessible region of potential. Normal rat and human urine were free from polarographic waves only over the region −0·2 to −0·7 volt. Moreover, the slope of the residual current and the oscillations due to growth and fall of drops were much greater than usual.

Accordingly, polarograms of known concentrations of 1314 *TH* in the above sera and cerebrospinal fluid were recorded and a well-defined wave of height proportional to concentration was obtained. There appeared to be no appreciable change of half-wave potential between serum solutions and aqueous solutions of the same *p*H. There was no need to add any extra supporting electrolyte or buffering agent beyond that already contained in the fluid. The limit of sensitivity with present equipment is ~0·2 μgm./ml. but it is hoped that this can be improved by suitable instrumentation. It was necessary to acidify the urine in order to bring the 1314 *TH* wave into the accessible region of potential, and addition of 5 per cent by volume of glacial acetic acid was a suitable procedure. The sensitivity was decreased to about 5 μgm./ml. because of the larger residual current. The polarographic method has been applied to serum, cerebrospinal fluid and urine from patients receiving 1314 *TH*.

Although most of the work on this problem has been devoted to the estimation of 1314 *TH* there seems no reason why any compound should not be estimated, the half-wave potential of which is in the accessible regions of potential and which does not interact significantly with serum proteins. Other compounds studied briefly in these laboratories to which the direct polarographic method can probably be applied are: pyrazine-2-carboxyamide, certain nitrofuran derivatives, *iso*nicotinylhydrazide and terramycin. The latter two drugs possess half-wave potentials close to the negative limit of accessible potential for serum, and some *p*H adjustment may be necessary to obtain highest sensitivities.

Since this preliminary communication was written, my attention has been directed to the work of Teisinger[1] on the direct polarographic determination of nitrobenzene in serum quoted by Brezina and Zuman[2]. It appears that the approach described above is not novel but has lain in abeyance for some twenty years.

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Effect of Azaserine (*o*-Diazoacetyl-L-serine) on the Pyridine Nucleotide Levels of Mouse Liver

THE amount of diphosphopyridine nucleotide in mouse liver has been shown to increase upon the intraperitoneal injection of a number of pyridine derivatives[1,2]; nicotinamide is the most effective, raising the level 8–10 times. Although nicotinic acid is as effective as many of the analogues, it appears to inhibit the synthesis when administered with nicotinamide, as compared with nicotinamide alone. Inhibition of synthesis from nicotinamide injection has also been reported with the administration of the purine antagonists 6-mercaptopurine and thioguanine[1,3]. These inhibitions appear to affect only the level of diphosphopyridine nucleotide attained from nicotinamide injection and the rate of its subsequent return to the normal level, but do not appear to affect the basal level normally found in the liver.

Recently, the injection of azaserine has been shown to inhibit markedly diphosphopyridine nucleotide synthesis resulting from nicotinamide injection[4]. Unlike the effects of the other inhibitors of this system, the administration of azaserine alone causes a marked reduction in the normal levels of the pyridine nucleotide.

We have found that subcutaneous injection of azaserine at a dosage of 200 mgm./kgm. rapidly reduces the level of pyridine nucleotide in the liver. The diphosphopyridine nucleotide-levels in the livers of 2–3 months old (*BALB/cAN* × *DBA/2J*) F_1 hybrid mice were followed using the methylethyl ketone method previously described[1]. In Fig. 1, it can be seen that the pyridine nucleotide-level drops to a minimum value, which is about a nine-fold decrease from the level in control mice injected with 0·85 per cent saline, in 1–2 hr.

After reaching a minimum value, the pyridine nucleotide content was found to rise slowly over a 24-hr. period, approaching the level of the saline-injected, control animal. It appears that this dosage is somewhat toxic with approximately 25 per cent of the animals dying between 20 and 24 hr. after injection of azaserine.

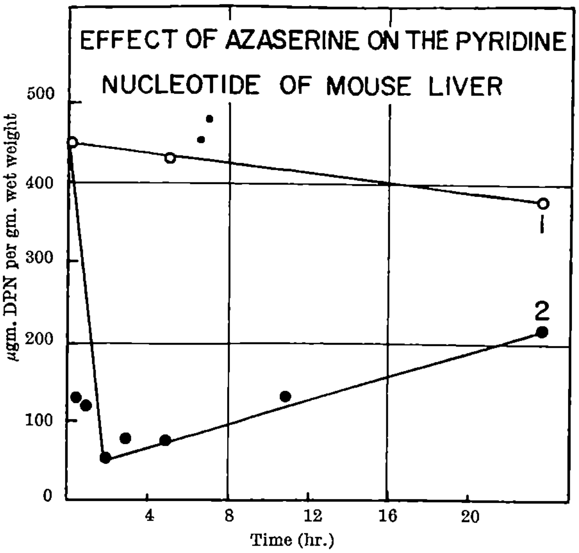

Fig. 1. Effect of azaserine on the pyridine nucleotide level of mouse liver. Determinations were made on a 5 per cent (w/w) trichloracetic acid extract of mouse liver. Each value represents the pooled samples of two mice. Curve 1, saline control; curve 2, azaserine-injected animals

Since the increase in diphosphopyridine nucleotide resulting from nicotinamide administration occurs mainly in the soluble fraction of the mouse liver, it was of interest to determine whether the azaserine reduction acts only on the soluble fraction. Accordingly, four animals were killed 1 hr. after azaserine injection, the livers homogenized in 0·25 *M* sucrose–0·05 *M* nicotinamide solution, pooled, and fractionated according to the method of Jacobson and Kaplan[5]. The results of this experiment, together with the values of the pyridine nucleotide content of livers of saline-injected animals treated similarly are compared in Table 1. Although the soluble fraction shows the greatest change in oxidized nucleotide content, the non-soluble fractions are lower, possibly indicating some equilibrium between the bound and soluble forms in the liver. There does not appear, however, to be an appreciable decrease in the reduced pyridine nucleotide.

Azaserine as well as 6-diazo-5-oxo-L-norleucine has been shown to inhibit synthesis of nucleotide precursors of diphosphopyridine nucleotide[6]. Accordingly, we have found that 6-diazo-5-oxo-L-norleucine behaved similarly to azaserine in lowering mouse liver diphosphopyridine nucleotide.

Inhibition of the precursors of pyridine nucleotide, either by the mechanism described above[6] or one similar to the system reported in red blood cells (also shown to be inhibited by azaserine[7]), would obviously result in a lowered diphosphopyridine nucleotide content of the liver. However, the rate of diphosphopyridine nucleotide destruction in mouse liver as indicated by radioactive experiments[4] cannot in itself account for the rapid decline of diphosphopyridine nucleotide that we have observed after azaserine administration. Furthermore, we have been unable to detect any destruction of diphosphopyridine nucleotide by azaserine under physiological conditions, nor have we observed increased activities of purified veal brain or *Neurospora crassa* diphosphopyridine nucleotidases when they were treated with azaserine. In fact the latter enzyme appears to be inhibited in the presence of high concentrations of azaserine.

Table 1. DISTRIBUTION OF PYRIDINE NUCLEOTIDES IN MOUSE LIVER HOMOGENATES

	µgm./gm. wet weight	
	Control	Azaserine injected
Oxidized		
Total homogenate	477	126
Nuclei	18·2	17
Mitochondria	23·7	12
Microsomes	14·8	8·2
Soluble	360	77·5
Reduced		
Total homogenate	260	198

Mouse livers were removed 1 hr. after azaserine injection. Controls were injected with saline. The values represent the pooled samples of four mice in each group.

Additional investigations are now being carried out in this laboratory in an effort to explain the above observations, and it is hoped that these studies will be of value in elucidating the pathway of diphosphopyridine nucleotide synthesis and its regulation in the intact animal.

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Reversal of Epinephrine Inhibition of Liver Tyrosine Oxidation

THYROID hormone interacts with the rat liver tyrosine oxidase system *in vitro* and *in vivo*[1]. The site of the inhibition proved to be at the first enzymatic step of the system, namely, tyrosine-α-ketoglutarate transaminase[1,2]. Canellakis and Cohen[3] first demonstrated an inhibition of this enzyme by epinephrine, using the enzyme from dog liver. Since, under certain conditions, thyroxin and epinephrine are metabolically related[4], it seemed likely that a demonstration of a similar action of both these hormones on the same enzyme system might provide a basis for exposing a mechanism of hormone action. Some empirical effects of epinephrine upon blood amino-acid levels are known[5-7]; but virtually no attempts have been made to explain these results at the molecular level.

The effects of treating a soluble cytoplasmic tyrosine oxidase preparation from rat liver[8] with increasing

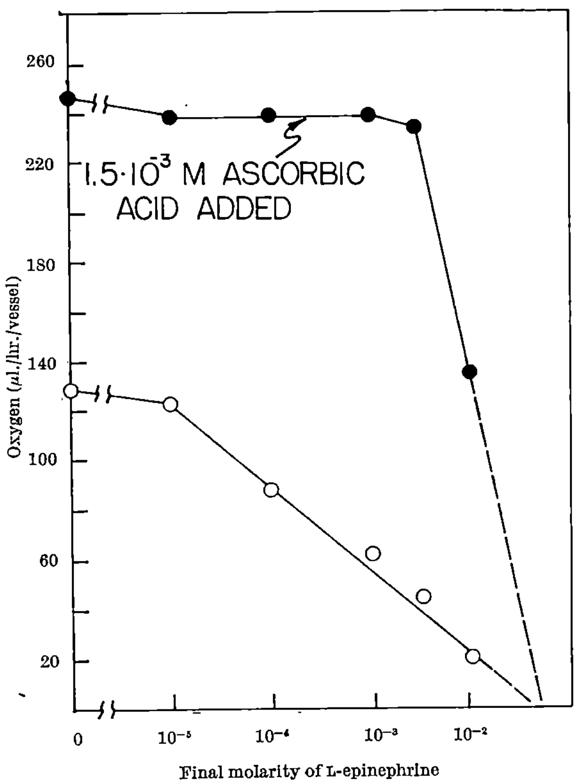

Fig. 1. Reversal of epinephrine-inhibited tyrosine oxidase. Open circles denote control curve without ascorbic acid; solid circles denote addition of $1 \cdot 5 \times 10^{-3} M$ ascorbate to each system. Epinephrine was incubated with the enzyme for 10 min. at 37° C. prior to addition of the substrate

concentrations of L-epinephrine showed that complete inhibition would occur at a level of $5 \times 10^{-2} M$ epinephrine compared with a saturation-level of L-tyrosine co-substrate of about $2 \times 10^{-3} M$. Fractionation of the overall 5-step system into single, double, or triple enzyme sub-systems, using appropriate substrates[8], revealed that inhibition by epinephrine occurs only when tyrosine and α-ketoglutarate are metabolized compared with *p*-hydroxyphenylpyruvate or homogentisate oxidation-rates. This confirmed that the initial enzyme participates in the reaction[3]. Partially purified homogentisate oxidase[9], on the other hand, is usually stimulated by the addition of epinephrine, presumably due to a redox property of the hormone. Complete reversal of epinephrine inhibition of tyrosine oxidation is accomplished by $1 \cdot 5 \times 10^{-3} M$ ascorbate with as much as $5 \times 10^{-3} M$ epinephrine added to the system (Fig. 1). The effectiveness of the vitamin decreases with higher concentrations of the hormone. It is unlikely that ascorbate functions by reducing the stability of epinephrine[10] to an appreciable extent in a system of this *p*H. It seems possible, however, that a chelate may be formed with an essential component and reversed by ascorbate although no evidence is available, as yet, on this point. Other redox agents which stimulate enzymes in the overall system, such as reduced glutathione[11] and dichlorophenolindophenol[12], fail to reverse the hormonal inhibition. Both norepinephrine and adrenochrome are inhibitors. Complete inhibition (extrapolation) occurs at $10^{-2} M$ L-norepinephrine. Only a slight reversal of norepinephrine inhibition is obtained by adding ascorbate to the system in concentrations up to $3 \times 10^{-3} M$. In every case the system can be partially protected by the tyrosine co-substrate if it is incubated with the enzyme prior to addition of the inhibitor. Pyridoxal phosphate, up to $5 \times 10^{-3} M$, fails to reverse epinephrine inhibition of the whole system. That the reversal of epinephrine inhibition by ascorbic acid involves the initial transaminase step is shown by the results in Table 1, where the oxidation-rates of tyrosine and *p*-hydroxyphenylpyruvate in the presence or absence of inhibitor and reversing agent are compared. Compounds such as ascorbyl palmitate, D-*iso*-ascorbate and ferrous ascorbate are as effective as ascorbic acid, but ferrous ion alone does not reverse epinephrine inhibition of the transaminase.

Table 1. RESULTS OF A TYPICAL MANOMETRIC EXPERIMENT SHOWING THE REVERSAL OF EPINEPHRINE INHIBITION TO OCCUR AT THE INITIAL TRANSAMINASE STEP

Substrate ($6 \mu M$)	Addition	Corrected enzyme activity (µl. O_2/hr./flask)	Inhibition (per cent)
L-Tyrosine*		87	
,,	$1 \cdot 5 \times 10^{-3} M$ ascorbate (AA)	169†	
,,	$1 \times 10^{-3} M$ L-epinephrine (EP)	35	58
,,	AA + EP	162	
Keto-*p*-HPP		52	
,,	AA	123†	
,,	EP	50	0
,,	AA + EP	109	

* α-Ketoglutarate present; α-ketoglutarate not added when *p*-hydroxyphenylpyruvate (HPP) is substrate.

† The increase in activity due to addition of ascorbate results from the effect of ascorbate upon homogentisate oxidase (ref. 8).

Physiological significance of this interaction is suggested by *in vivo* experiments which show that intraperitoneal injections of L-epinephrine (1 mgm./kgm. body-weight for 1 hr.), compared with saline-injected rats, produce a 55 per cent inhibition of specific enzyme activity. Addition of $1 \cdot 5 \times 10^{-3} M$ ascorbate *in vitro* causes twice the stimulation of control specific activity in preparations derived from epinephrine-treated animals compared with saline-injected animals. Details and extension of this work will be presented elsewhere.

This investigation was supported in part by a research grant, *A*–1919, from the National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Public Health Service. The homogentisic acid used was isolated from urine of alkaptonuric patients and generously provided by Dr. B. N. La Du, jun., National Institute of Arthritis and Metabolic Diseases, National Institutes of Health.

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Purification of Neuraminidase from *Vibrio cholerae*

Blix, Gottschalk, and Klenk[1] proposed the name 'neuraminidase' for the enzyme which splits the glycosidic linkage joining terminal (substituted or unsubstituted) neuraminic acid to residual oligo- or poly-saccharide. Kuhn and Brossmer[2] and recently Gottschalk and Graham[3] have isolated well-defined substrates by which the enzymatic action of neuraminidase could be studied. There exist many other substrates of high molecular weight and unknown structure; for example, mucoproteins from urine, saliva, serum, or stromata of erythrocytes. Neuraminidase is present in viruses of the myxo-group (influenza, fowl plague, Newcastle disease, mumps) and was found in filtrates of *Vibrio cholerae*[4] and *Clostridium welchii*[5].

To clarify the function of neuraminidase for the virus – host cell relationship it would be desirable to study the structure of the enzyme. Since virus material is not available in sufficient amounts an attempt was made to isolate the enzyme from the culture fluids of *Vibrio cholerae*.

In order to control the purification of the enzyme, a simple method for serial determinations was developed. The basis of this determination is the splitting of neuraminic acid (or its acyl derivative) from a standard substrate. Mucoprotein from human urine was used as standard, which was prepared by a modification of the method of Tamm and Horsfall[6]. Stromata of erythrocytes from sheep or calves were also found to be suitable.

The activity of neuraminidase was measured in the following way. 4 mgm. of urinary mucine containing 3·8–4·1 per cent neuraminic acid was dissolved in 1 ml. water. The enzyme solution (0·001–0·2 ml.) was added and the total volume made up to 2 ml. with 0·1 *M* acetate buffer at *p*H 5·5. This mixture was incubated for 15 min. at 37° C. The reaction was stopped by precipitation of the mucine with 2 ml. of a saturated solution of benzoic acid in chloroform (65 gm./100 ml.). After vigorous shaking, the solution was centrifuged at 3,500 r.p.m. for 4 min. The mucine forms a layer between the chloroform and the supernatant aqueous solution. From the clear supernatant solution 1 ml. was used for the determination of the liberated neuraminic acid by the orcin reaction according to Böhm, Dauber, and Baumeister[7]. A reference curve was obtained using crystalline methoxy-neuraminic acid, kindly supplied by Prof. E. Klenk. The quantity of the enzyme should be adapted in such a way that 8–20 μgm. of neuraminic acid are liberated. The unit *E* of enzyme activity was defined as that amount which liberates 1 μgm. of neuraminic acid in 15 min. at 37° C. under the conditions described. The purity of the enzyme is measured by the specific activity *E*/μgm. protein nitrogen. The nitrogen was determined by the Kjeldahl method if sufficient material was available; otherwise the preparation was hydrolysed by 6 *N* hydrochloric acid and the amino nitrogen was determined by ninhydrin by the method of Stein and Moore[8].

Filtrates of *Vibrio cholerae* cultures supplied by Behring-Werke, Marburg, were used as the starting material. The specific activity could be increased 50,000-fold by a relatively simple procedure. At the beginning of this work, enzyme instability caused certain difficulties. The purified enzyme sometimes lost its activity within a few hours. Sufficient stabilization could be achieved, however, by employing chelating agents. Addition of cyanide was particularly effective during purification, but the enzyme can also be stabilized by serum albumin and other proteins.

Table 1. PURIFICATION OF NEURAMINIDASE

Fraction	Activity (*E*/ml.)	Specific activity (*E*./μgm. nitrogen)	Purification factor
1. *Vibrio cholerae* filtrate	30–60	0·01–0·03	1
2. Concentrate after elution from erythrocytes	200–300	1–2	100
3. Eluate from column chromatography	300–500	120–130	6,000
4. After precipitation with ammonium sulphate	20,000–100,000	1,000	50,000

The first step in purification was the concentration of neuraminidase by adsorption to sheep erythrocytes at *p*H 8–9, followed by an elution at *p*H 5·5, in a way similar to that described by Burnet[4]. Since hæmolysis cannot be avoided, the preparation is heavily contaminated with hæmoglobin.

The following step is the most significant. It may also be useful for the purification of other enzymes which have a high affinity for their specific substrate. This step combines the specific binding of the enzyme to its substrate with column chromatography. Stromata of erythrocytes from sheep or calf, prepared by two-fold hæmolysis, were used as substrate. They were mixed with kieselgur (Merck) to form a chromatographic column. The enzyme was adsorbed at 0° C., *p*H 9 in a buffer containing 0·01 *M* borate, 0·9 per cent sodium chloride and 0·1 per cent calcium chloride. The contaminating hæmoglobin and other proteins were washed out with the same buffer, and the enzyme was eluted at *p*H 5·5 at 0° C. In the adsorption buffer, the enzyme is firmly bound to the substrate, whereas in the acidic medium the substrate is split and the enzyme released.

The eluate from the column was concentrated over phosphorus pentoxide after addition of potassium cyanide. For further purification, the enzyme can be precipitated from the concentrate by half saturation with ammonium sulphate. On the other hand, if a solution containing a lower concentration of ammonium sulphate is slowly evaporated, a protein containing the total enzyme activity is crystallized out in needles.

The concentration of the enzyme and the increase in specific activity during the purification process is shown in Table 1. The purification was repeated several times. In each step of the procedure, 70–80 per cent of the activity was recovered. From the values in Table 1, it may be calculated that the starting material contains 50 μgm. enzyme nitrogen or 300 μgm. enzyme protein per litre. 12 l. of *Vibrio cholerae* filtrate were used in order to obtain sufficient material for ultra-centrifuge studies.

The purified protein is sedimented down with a fairly homogeneous boundary. A sedimentation constant of about $s_{20} = 1{\cdot}3$ S. was measured at *p*H 8·5 in a solution containing 0·02 *M* potassium cyanide. From this value a molecular weight of 10–20,000 is estimated, assuming a spherical shape. Boundaries with higher sedimentation constants were observed under other conditions, suggesting that the protein has a tendency to aggregate. Evidence for the identity of the isolated protein with the enzyme is based on the high specific activity of the protein and the specificity of the purification procedure. Furthermore, it was found that the sedimentation of enzyme activity, measured by the decrease in enzyme activity in the supernatant, was of the same order as the sedimentation constant of the boundary in the ultracentrifuge. Finally, in the purified preparations, proteinases were no longer detectable.

The reaction kinetics of the enzyme was studied in some detail. A Michaelis constant of about $1–2 \times 10^{-4}$ mole neuraminic acid/l. was determined using sheep stromata as substrate. This confirms the high affinity of the neuraminidase for the specific substrate, which made possible the specific purification procedure described here.

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Asymmetric Hydrolysis of Diethyl Acetamidomalonate by Chymotrypsin

CONTINUING our study[1] of asymmetry in reactions of non-asymmetric molecules of the type *Ca,b,d,d*, we are examining the hydrolysis of diethyl acetamidomalonate $CH_3CONHCH(COOC_2H_5)_2$ by chymotrypsin. The ester (Matheson) was crystallized from benzene–petroleum ether, m.p. 96·5–98° C. Chymotrypsin was from Worthington, salt free, lot *CD* 576–81. The kinetics of hydrolysis were studied in water at 25°, with magnetic stirring, in the *p*H range 7·0–7·95 with *tris*hydroxymethylaminomethane ($3 \cdot 3 \times 10^{-3}$ *M*) or phosphate ($8 \cdot 3 \times 10^{-3}$ and $1 \cdot 6 \times 10^{-2}$ *M*) buffers. Runs were carried out with a Beckman model *G p*H meter, 0·1 *N* sodium hydroxide being added from a Gilmont micro pipette-burette to maintain the *p*H, or, at high enzyme concentrations, with a *p*H-stat, radiometer titrator and automatic burette delivering 0·4 *N* sodium hydroxide.

The hydrolysis was first order in the ester and the rate 'constants' k_1 were proportional to enzyme concentration (Table 1). The reaction stopped after liberation of one equivalent of acid. The ester was quite stable in the absence of enzyme, its hydrolysis in $3 \cdot 3 \times 10^{-3}$ *M* buffer at *p*H 7·8 showing an apparent k, of 0·0004 min.$^{-1}$. The hydrolysis is first order in both substrate and enzyme under these conditions.

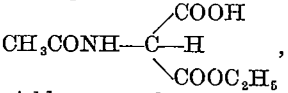
The product of one run, 20 ml. initially 0·02 *M* in the ester was dialysed against 0·001 *N* hydrochloric acid and this was extracted with ether leading to 2-acetamido-2-carbethoxyacetic acid  $CH_3CONH{-}C(COOH)(H)(COOC_2H_5)$, 0·053 gm., 70 per cent yield; m.p. from benzene–ethanol 138–139° dec.; mixed m.p. 139–141°, synthetic sample 140–141°, reported[2] 140–141·5°.

Table 1. HYDROLYSIS OF DIETHYL ACETAMIDOMALONATE BY CHYMOTRYPSIN AT *p*H 7·8 ± 0·15

Chymotrypsin (mgm./ml.)	Ester (*M*)	k_1 (min.$^{-1}$)
0·39	0·0046	0·016 ± 0·001
0·39	0·0092	0·016 ± 0·001
0·39	0·0200	0·016 ± 0·001
0·50	0·0200	0·020
0·10	0·0200	0·042
1·69	0·0637	0·067

The product of a run, carried out in the *p*H-stat at 7·8, with 0·05 *M* ester, an enzyme concentration of 0·91 mgm./ml., and 0·0069 *M* phosphate, was examined in a Zeiss–Winkel polarimeter after 3 hr. reaction, one equivalent of acid having been generated, and was found to be optically active, $\alpha_{obs.} + 1 \cdot 77° \pm 0 \cdot 03$ (after minor correction for chymotrypsin), $[\alpha]^{22}_D + 63° \pm 2$ for the half-ester, based on its presence in quantitative yield as one enantiomorph (the value is not inconsistent with those reported for some derivatives of monosubstituted malonic acids[3]). The rotation fell with time reaching half its original value in about 44 hr. The product of another run carried out with 0·016 *M* phosphate and not examined as quickly led to $[\alpha]^{22}_D$, + 59°. When the hydrolysis was followed in the polarimeter, necessarily in more concentrated (1 *M*) buffer, the rotation rose initially ($\alpha_{obs.}$, + 1·55°) and then fell in 4 hr. to the reading of the blank.

The ester, unlike the related diethyl benzylmalonate, which is rather inert[4] to chymotrypsin under comparable conditions, is hydrolysed by this enzyme to the half-ester. The observed optical activity indicated that this enzyme distinguishes between the two similar ester groups in diethyl acetamidomalonate and that the half-ester is formed optically active and racemized during isolation, presumably by enolization (this kind of steric selectivity has been demonstrated by use of tissue homogenates for citric acid[5] and for glycerol[6]). Isolation of the optically active half-ester is now being attempted. These experiments indicate that the related aminomalonic acid, which is decarboxylated enzymatically[7], may be found to do so asymmetrically, as has been suggested[8], and as would be required by the results of conversion of serine, labelled isotopically in nitrogen and carboxyl carbon, to glycine[9], if aminomalonic acid is to be an intermediate in this process. This is indicated also by reactions of methylmalonic acid[10].

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Reduced Diphosphopyridine Nucleotide—Neotetrazolium Reductase

Martius[1] has reported the presence in animal tissues of a quinone reductase (phylloquinone reductase) similar in properties to menadione reductase described by Wosilait and Nason[2]. Phylloquinone reductase couples the oxidation of reduced diphosphopyridine nucleotide (DPNH) with the reduction of vitamin K_3. Since the reduced form of vitamin K_3 reduces neotetrazolium chloride (NT) directly to the coloured insoluble formazan[3], it is of interest to investigate the production of formazan by the enzymic oxidation of reduced diphosphopyridine nucleotide in order to ascertain if this enzymic sequence involves a quinone reductase. In this communication the enzymic process linking the oxidation of reduced diphosphopyridine nucleotide with reduction of neotetrazolium chloride is termed DPNH–NT reductase.

Liver homogenates were prepared either in water or in 0·25 *M* sucrose at 0° C., using a conventional Potter–Elvehjem type homogenizer. The animals used were adult female rats of the Medical Research Council strain, body-weight 180–200 gm.

DPNH–NT reductase was assayed by incubating aerobically 0–20 mgm. wet weight tissue with 1 ml. phosphate buffer (*p*H 7·4, 0·1 *M*), substrate (reduced diphosphopyridine nucleotide, or diphosphopyridine nucleotide plus β-hydroxybutyrate) and 0·15 ml. of 1 per cent neotetrazolium chloride. Buffer, tissue and substrate were pre-incubated for 2 min. at 37° C. aerobically before the addition of neotetrazolium chloride. The reaction was stopped by the addition of 1 ml. of 10 per cent trichloracetic acid; the formazan was extracted with 4 ml. of ethyl acetate. The extinction at 510 mµ was obtained using a Hilger 'Uvispek' spectrophotometer. When other additions were made to the reaction mixture (see Table 1), the reagent added was usually incubated with buffer plus tissue for 15–30 min. at 0° C. Except in those experiments involving differential centrifuging all tissue suspensions were prepared in water to reduce the possibility of permeability phenomena arising with mitochondrial enzymes.

The addition of reduced diphosphopyridine nucleotide (0–1·0 µmole) or of diphosphopyridine nucleotide (0–1·0 µmole) plus β-hydroxybutyrate (final concentration 0·01 *M*) to the incubation mixture led to rapid production of formazan with liver suspensions (Fig. 1). The effects of adding vitamins K_1 and K_3 are also shown in Fig. 1; both vitamins were added in suspension as described elsewhere[4].

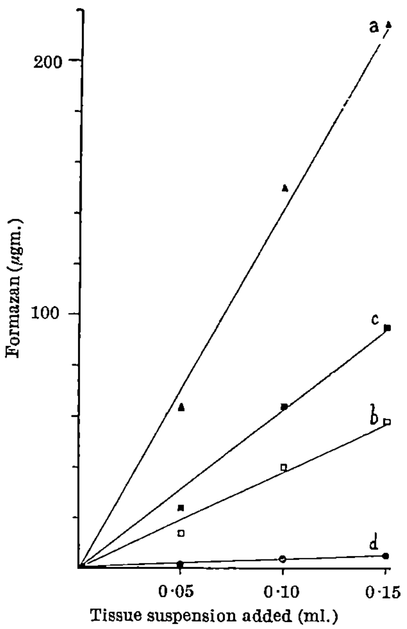

Fig. 1. Formazan production by rat liver tissue suspensions; diphosphopyridine nucleotide + β-hydroxybutyrate as substrate. Curve (*a*), 100 mgm. wet weight tissue/ml.; 1 µmole diphosphopyridine nucleotide; incubation, 10 min. Curves (*b*), (*c*) and (*d*), mitochondrial suspension (1 : 5) frozen and thawed three times; incubation, 15 min.; diphosphopyridine nucleotide, 0·5 µmole; further additions: curve (*b*), 0·1 ml. phosphate/ethanol/plasma albumin suspension; curve (*c*), 0·1 ml. vitamin K_1 (0·3 µmole added) in phosphate/ethanol/plasma albumin; curve (*d*), 0·1 ml. vitamin K_3 (0·8 µmole added) in phosphate/ethanol/plasma albumin

Table 1. ACTION OF VARIOUS INHIBITORS, UNCOUPLING AGENTS, QUINONES AND VITAMINS ON DPNH–NT REDUCTASE

Substrate	Addition (in 0·1 ml.)		Formazan production as percentage of control value
	Substance	Amount (µmoles)	
DPN + BHB*	amytal	2·0	102
DPNH	amytal	12·8	94
DPNH	QMS	5·0	97
DPNH	QMS	10·0	78
DPNH	QMS (anaerobic)	10·0	84
DPNH	quinine sulphate	1·0	100
DPNH	azide	20·0	97
DPNH	versene	20·0	93
DPNH	α,α′-dipyridyl	2·0	92
DPNH	α,α′-dipyridyl	25·0	98
DPN + BHB	manganous chloride	0·4	60
DPNH	manganous chloride	0·4	65
DPN + BHB	2.4-dinitrophenol	0·2	75
DPNH	2.4-dinitrophenol	0·1	95
DPN + BHB	dicoumerol	1·2	43
DPNH	dicoumerol	1·2	20
DPNH	1.4-naphthaquinone	2·0	7
DPN + BHB	vitamin K_3	1·0	21
DPNH	vitamin K_3	1·0	45
DPN + BHB	vitamin K_1	0·3	182
DPNH	vitamin K_1	0·6	111
DPNH	PCMB	1·0	5

* BHB, β-hydroxybutyrate.

Previous reports have indicated that enzymic reduction of tetrazolium salts occurs via a flavoprotein[5]; in an attempt to investigate this possibility the effects of several types of inhibitor were studied. The results are shown in Table 1. It can be seen that sodium amytal, quinine sulphate, α-α′-dipyridyl, sodium azide and sodium versenate had no appreciable effect on DPNH–NT reductase. Quinacrine methane sulphonate (QMS) was inhibitory only in high final concentration both under aerobic and anaerobic conditions. The sulphydryl-reagent *p*-chloromercuribenzoate (PCMB) was strongly inhibitory, as were quinones like 1.4-naphthaquinone, vitamin K_3, and the natural quinone antagonist dicoumerol. Vitamin K_1 was, however, stimulatory in low final concentration. DPNH–NT reductase was inhibited in a variable manner by manganous chloride and by 2.4-dinitrophenol, both of which are known to uncouple oxidative phosphorylation. 2.4-dinitrophenol has also been reported to inhibit quinone reductase and menadione reductase[2].

The results suggest that DPNH–NT reductase, which is an extremely active enzyme in rat liver, does not contain an easily dissociable flavoenzyme complex which would presumably be strongly inhibited by quinine sulphate or quinacrine methane sulphonate. Wosilait and Nason[2] reported that quinacrine produced no inhibition on menadione reductase. It would appear then that if DPNH–NT reductase contains a functional flavoenzyme the flavine group is strongly bound to the protein. A lack of inhibition by quinacrine is not unequivocal evidence for the absence of a functional flavoenzyme.

DPNH–NT reductase does not appear to utilize the amytal-sensitive route connecting oxidation of reduced diphosphopyridine nucleotide with the cytochrome chain[6]. However, it would seem that DPNH–NT reductase involves a quinone structure similar in properties to vitamin K_1 and which can be inhibited by both vitamin K_3 and dicoumerol. The effects of vitamins K_1 and K_3 on DPNH–NT reductase are the reverse of those found for succinate–neotetrazolium chloride reductase[4] but are analogous to the effects of vitamins K_1 and K_3 on oxidative phosphorylation[7]. The effects of such quinones as 1,4-naphthaquinone and vitamin K_3 on DPNH–NT reductase are being investigated further to ascertain if their inhibitory power is an unspecific redox property or is the result of competitive inhibition with another quinone structure.

Using sucrose homogenates the distribution of DPNH–NT reductase in intracellular fractions was investigated. The following centrifugal accelerations for the times indicated were used to separate each fraction: (*a*) nuclear fraction, 600*g* × 10 min.; (*b*) mitochondrial fraction, 10,000*g* × 15 min.; (*c*) microsomal fraction, 105,000*g* × 30 min. The reductase appears to be largely associated with the mitochondrial and microsomal fractions. In a typical experiment the percentage of the total activity associated with each fraction was: nuclear, 8; mitochondrial, 60; microsomal, 28; and soluble fraction, 3.

I am grateful to Dr. A. L. Greenbaum and D. N. Planterose for many helpful comments. The work was done during the tenure of a Beit Memorial Fellowship.

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Carotene Content of *Ulex europaeus* (Common Furze)

A GENERAL investigation has been in progress for some time in this Department into certain aspects of the chemistry of *Ulex europaeus*. This common furze has a local reputation as a supplementary animal foodstuff, while it has also been reported from France as a suitable fodder for sheep[1].

The analytical results (mean percentages) from air-dried samples of furze growing on waste land in County Cork during the past year are as follows: moisture, 18·4; crude protein, 10·2; fibre, 26·6; fat, 1·2; nitrogen-free extract, 41 ; inorganic matter, 2·6.

No previous results are available on the carotene content of the green matter (spines) of furze and its seasonal variation, which are now reported. The following procedure has been followed in making the determinations on fresh plant material.

The furze bushes were collected in the mornings; the green, prickly spines were taken for analysis and the main woody portion of the plant discarded. The spines were chopped as soon as possible after picking. Representative samples were blanched for 1 min. in boiling water[2] and stored in a frozen condition when analysis was not immediately undertaken. Losses of carotene of up to 15 per cent were recorded when unblanched samples were analysed after 1 hr. storage. The procedure also facilitated extraction of the pigments.

The furze samples were treated with a 3 : 2 mixture of acetone–petroleum ether (boiling point, 40–60° C.) for 2 min. in a high-speed 'blendor' fitted with a small baffle-plate[3]. Calcium carbonate, just sufficient to neutralize plant acids, was added[4]. The extract was filtered, the entire process repeated twice more and acetone washed from the bulked solvent solution with water. Three processings were found to be sufficient as analysis of residues yielded no pigments.

The petroleum ether solutions were chromatographed on 10 cm. × 1·5 cm. columns of either, (1) a mixture of equal parts of magnesium oxide ('Sea Sorb 43' Fischer) and 'Hyflo-Super Cel' Johns-Manville[5], or (ii) alumina[6]. In both cases the columns were topped by a 2-cm. layer of anhydrous sodium sulphate. Carotene was eluted with 4 per cent ether in petroleum ether. Elution could be followed visually and its completion readily gauged. The eluate was made up to volume and its absorption measured on a Beckman spectrophotometer (model *D.U.*). Control analyses showed quantitative recovery of carotene added to furze samples.

The variation in carotene content of furze over a year's survey is shown in Table 1.

Table 1

Month	Carotene (mgm./kgm. dry weight)	Month	Carotene (mgm./kgm. dry weight)
January	124	July	253
February	125	August	230
March	134	September	138
April	159	October	147
May	171	November	120
June	235	December	101

Separation of the carotene mixture showed that β-carotene was the main constituent, up to 95 per cent of the total.

From October to February or March—when furze is fed to stock—the average carotene content is 126 mgm./kgm., indicating that it is a very good, and freely available, source of carotene. The relatively high values during the summer months point to the possibility of using dried furze meal as a supplementary source of carotene in animal feeding.

The problem of retention of carotene in dried furze is being investigated concurrently with that of the amino-acids in the furze protein, and a detailed report will be published later.

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PHYSIOLOGY

Elongation of Rat-Tail Tendon on Hydration

The extent of hydration in connective tissues is of considerable physiological importance. Water retained by mucopolysaccharides and collagen is thought to have a pronounced effect upon the mechanical functioning of the tissue[1]. The rate and extent of swelling of collagen[2] were studied in order to measure the hydration of collagen as well as to ascertain how this might be related to the degree of cross-linking of the protein. The objective of the work discussed here was to analyse the rate and extent of elongation of a dry tendon when it was immersed in solutions.

Tendons were removed from rat tails, after stripping away the skin, by the usual method of blunt dissection with a pair of pliers. They were washed three times in 50 ml. of 0·1 *M* sodium chloride solution then washed continuously with distilled water for 30 min. Within half an hour of exposure to a temperature of 22–25° C., the tendons dehydrated to a constant ratio (*W*) of weight/length. A single tendon was inserted in a 10-ml. syringe cylinder through the bore of the glass tip ; one end was immobilized by forcing a three-way adapter over the tip while the other end, 10 cm. distant, was attached to a mechanical lever system by a small 'Alligator' clip. A 70-cm. lever arm having a mechanical ratio of 20 was used to record the elongation on an electrically driven kymograph. The load on the tendon was 20 gm. throughout the entire process.

Upon the addition of water the length increased from an initial 'dry' value (L_0) to a steady-state value (L_0+L_∞) in about 1 min. At this point the water was removed and air was sucked through the cylinder. The tendon was allowed to dry for 20 min. at a constant temperature while it shortened to (L_0) with a change in length (L_∞) of 2–4 mm. A base line was then drawn on the kymograph, the elongation on hydration was restarted by adding water, and the increase in length recorded continuously until the steady-state length (L_0+L_∞) was reached. The process of elongation on hydration and contraction on dehydration could be reproduced at least 10 times without any apparent alteration in the response of the tendon.

The length – time curve for a typical hydration–elongation is shown in Fig. 1. The first derivative ($\Delta L/\Delta t$) is plotted on the same graph to show the relationship between a point of inflexion in the displacement curve and what might be a discontinuity in the velocity curve. When the first derivative was plotted against the quantity ($L_\infty - L$) a curve resulted similar to that obtained when it was plotted against *t*. When the first derivative was plotted against the quantity $(L_\infty - L)t$ a linear relationship was found :

$$dL/dt = K(L_\infty - L)t \qquad (1)$$

Here, dL/dt is the rate of change of the length of tendon during the hydration, *K* is a specific rate constant for the process, L_∞ is the maximum change in length attained, and *L* is the change in length at any particular time, *t*. Rearrangement of the terms in equation 1, followed by integration between the limits from zero to *L* in the time-interval from zero to *t*, gives equation 2 :

$$\log (L_\infty - L) = \log (L_\infty) - Kt^2/(2 \times 2{\cdot}303) \qquad (2)$$

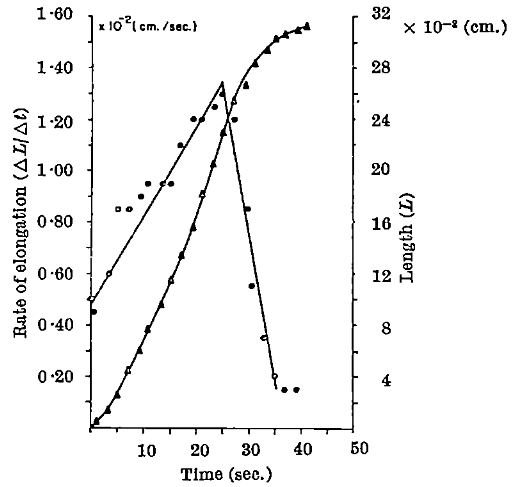

Fig. 1. The displacement (curve) and rate of displacement (straight lines) of a tendon during the hydration-elongation process. Water temperature is 23° C. and load is 20 gm.

Fig. 2 shows a family of curves plotted according to equation 2. The elongation on hydration of the same tendon was performed in water/methanol solutions where the composition was changed from 0 to 80 per cent methanol in steps of 10 per cent. The equation was obeyed satisfactorily for the elongation on hydration induced by the addition of water. However, mixed solvents produced an initial non-linear decrease in the term $\log (L_\infty - L)$ which after a short interval became linear with t^2. The extent of the deviation was minimal in water/methanol solutions but increased for other mixed solvents in the order methanol < ethanol < *iso*-propanol and propanol. The rate constant (*K*) was evaluated from the linear portion of the curve of the results with water/methanol shown in Fig. 2. Equation 3 shows a relation which was found to exist between *K* and the dielectric constant (*D*) of water/methanol solutions :

$$\log K = \log K_0 + B(D - 1)/(2D + 1) \qquad (3)$$

At concentrations of methanol greater than 40 per cent there was a positive deviation of the results indicative of specific solvent effects. It was found also that, over the region 0–80 per cent methanol, the

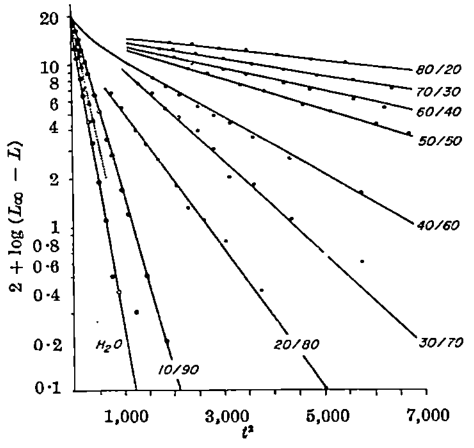

Fig. 2. The hydration-elongation of a tendon by water/methanol solutions ranging from 0 to 80 per cent methanol. The dotted line is a re-run of the water control after an 80 per cent methanol run. The initial non-linearity is shown as a curved line in an exaggerated form for the 40/60 composition

extent of elongation was related to the dielectric constant by expression 4:

$$\log (L_\infty) = \log (L_\infty)_{D=\infty} - C/D \quad (4)$$

The terms B and C, for simple reactions between ions and molecules in solution, are functions of their electrostatic interaction[3]. They might bear similar relationships to electrical interactions between charged units in the proteins of the tendon.

The rate constant (K) depends upon the diameter of the tendon and is related to it by the equation $K = K_0/W$. Since W is the ratio of weight/length, which is equivalent to $4\pi r^2 \times L \times$ density$/L$, the rate of elongation depends upon force/area, or tension.

This mechanico-chemical system offers a new method for studying the influence of the properties of solutions on a reaction between these solutions and the rat-tail tendon.

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Drug-induced Immunological Tolerance

PREVIOUS work in this laboratory demonstrated that administration of a purine analogue, 6-mercaptopurine, suppressed the antibody response to a soluble antigen (human serum albumin) in rabbits[1]. It was shown that the antimetabolite could block completely the primary immune response to the purified protein antigen; its effect on the secondary response, however, was minimal[2]. It is the purpose of this communication to describe the apparent induction of immunological tolerance in adult rabbits by the use of 6-mercaptopurine.

Adult New Zealand rabbits were given one intravenous injection of human serum albumin labelled with iodine-131; the disappearance of the labelled antigen from the plasma was determined by the method of Talmage *et al.*[3]. In the experimental group a daily intramuscular injection of 6-mercaptopurine (6 mgm./kgm.) was given beginning with the day of antigen injection and continued for two weeks. Control animals received only the labelled antigen. The human serum albumin disappeared from the circulation of the control group in the three phases described previously[3]; the onset of the immune disappearance phase occurred on the eighth day, and by the tenth day radioactivity (that is, antigen) could no longer be detected in the serums taken from this group. The animals treated with 6-mercaptopurine failed to develop an immune disappearance phase, and the antigen showed a logarithmic disappearance from the serum, similar to that seen after the injection of homologous albumin, thus indicating a failure to form antibody.

About one month after the first injection of antigen, both groups of rabbits were given a second injection of human serum albumin labelled with iodine-131. In addition, both groups were given 20 mgm. unlabelled bovine γ-globulin intravenously. No further 6-mercaptopurine was given. The control group developed a typical secondary response to human serum albumin (Table 1) and precipitating antibodies to human serum albumin and bovine γ-globulin appeared in their serums. The drug-treated group again showed a normal or logarithmic disappearance of labelled human serum albumin without any evidence of antibody formation to this antigen. Precipitating antibodies to bovine γ-globulin, however, were present in their serums.

Table 1. ANTIBODY LEVELS IN DRUG-INDUCED IMMUNOLOGICAL TOLERANCE (μGM. N/ML. SERUM)

		Day of experiment		
		14	48	80
Controls	Anti-human serum albumin	62	256	354
	Anti-bovine γ-globulin	—	107	288
Tolerant	Anti-human serum albumin	0	0	0
	Anti-bovine γ-globulin	—	94	242

About one month following the second injection of antigens, both groups were given a third injection of labelled human serum albumin together with a second injection of unlabelled bovine γ-globulin. Again, no 6-mercaptopurine was given. Both groups developed typical secondary responses to bovine γ-globulin. The human serum albumin was rapidly removed from the circulation of the control group, indicating the presence of humoral antibody to human serum albumin at the time of the third injection of that antigen. The group treated with the drug, however, again showed no evidence of anti-human serum albumin formation, as determined by the logarithmic disappearance of the labelled serum from the circulation, and by negative precipitin tests.

The term 'actively acquired tolerance', first used by Billingham, Brent and Medawar[4], was defined as "an induced, specific, central failure of immunological response brought about by an exposure of animals to antigenic stimuli *before maturation of the faculty of immunological response*" (italics ours). Tolerance of this type to homografted tissues and organs as well as to simpler antigens has been induced in laboratory animals by many workers[5]. In all such experiments, this has been carried out in the newly born or immature animal. The mechanism of this phenomenon is obscure; but the results of the present study indicate that the fœtal state is not essential for its induction. As a working hypothesis, we propose that the metabolic activity provoked in antibody-forming cells by antigenic substances, in addition to providing

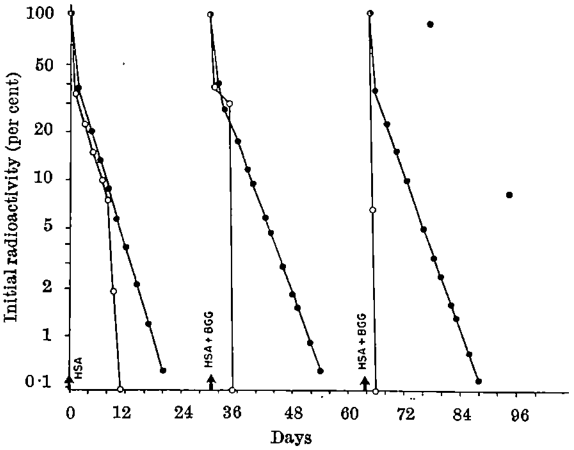

Fig. 1. Disappearance of human serum albumin labelled with iodine-131 in control and tolerant rabbits. ○, Controls; ●, animals treated with 6-mercaptopurine

Incorporation of 5-Iodouracil labelled with Iodine-131 into the Deoxyribonucleic Acid of Human Leukæmic Leucocytes following *in vivo* Administration of 5-Iododeoxyuridine labelled with Iodine-131

THE extensive introduction under cell culture conditions of 5-bromodeoxyuridine and 5-iododeoxyuridine into the deoxyribonucleic acid of a cell strain derived from a human tumour was recently reported[1,2]. Prusoff *et al.* and Mathias and Fischer[3-6] have recently reported *in vitro* and *in vivo* animal studies with 5-iododeoxyuridine. *In vivo* studies in this laboratory have been oriented towards possible uses of labelled 5-iododeoxyuridine in the investigation of nucleic acid metabolism of human leukæmic leucocytes as well as other tissues in which cell proliferation is extensive.

Experiments in animals showed that the labelled 5-iododeoxyuridine was incorporated to the extent of 0·5–1 per cent into the deoxyribonucleic acid fraction of intestine and tumour of rats bearing 7-day *H.S.* No. 1 and *H.Ep.* No. 3 human tumour transplants[7]. Toxic effects were not observed following daily administration of 5-iododeoxyuridine at 33 mgm./kgm. for one week in the mouse and two doses at 6·6 mgm./kgm. to a dog on successive days.

The incorporation of the labelled iodouracil moiety into the deoxyribonucleic acid of circulating leucocytes was measured following intravenous administration of 0·62 mc. labelled 5-iododeoxyuridine (9·6 mgm.) to a 44-year old, 85-kgm. woman with previously untreated chronic granulocytic leukæmia and enlarged spleen and liver (Table 1). Incorporation of iodine-131 into the thyroid was prevented by repeated administration of potassium iodide. Sodium nucleates were extracted from the washed white cells in hot salt solution. Following dialysis of this extract, the ribonucleic acid was hydrolysed in alkaline solution and the ribonucleotides, after neutralization, removed by a second dialysis. The deoxyribonucleic acid was hydrolysed to deoxyribonucleosides by treating an aliquot of the resulting solution with deoxyribonuclease (0·0025*M* magnesium sulphate, *p*H 7) at 37° for 5 hr. followed by addition of snake venom phosphoesterases for an additional 5 hr. [8]. After coagulation of protein at 100°, aliquots of the supernatant were subjected to descending paper chromatography in *iso*propanol/hydrochloric acid/water. Labelled 5-iododeoxyuridine and thymidine were eluted. The activity of the former was measured using a scintillation counter and the µmol. of the latter determined by ultra-violet absorption. The incorporation of labelled 5-iododeoxyuridine into the deoxyribonucleic acid is expressed in column 2 as counts per min. (c.p.m.) labelled 5-iododeoxyuridine/µmol. thymidine. The possibility of contamination was eliminated by paper chromatographic studies which showed that the labelled 5-iododeoxyuridine could be detected only after treatment with deoxyribonuclease and snake venom phosphoesterases. The major portion of the administered radioactivity was eliminated in the urine (column 3). Essentially all the radioactivity was present in the urine as labelled iodide ion with the exception of the initial 2-hr. collection, which contained 8 per cent of the total administered radioactivity. In this sample 11 per cent of the activity was present as labelled 5-iododeoxyuridine. In a previous experiment in the human, less than 1 per cent of the administered activity was present in the stool.

Table 1. INCORPORATION OF 5-IODODEOXYURIDINE LABELLED WITH IODINE-131 INTO THE DEOXYRIBONUCLEIC ACID OF CIRCULATING WHITE CELLS

Hours after administration	Deoxyribonucleic acid : c.p.m. 5-iododeoxyuridine/micromole of thymidine	Cumulative percentage excretion of iodine-131 in urine
24		53
48	$2 \cdot 7 \times 10^2$	67
120	$4 \cdot 9 \times 10^2$	72·1
168	$2 \cdot 0 \times 10^2$	72·4

The results at 120 hr. indicate that at least 1 per cent of the administered radioactivity was incorporated into the deoxyribonucleic acid of the leucocytes. This is based on a white cell count of $2 \cdot 5 \times 10^5$/mm.^{3} and the following assumed values: 6 l. estimated blood volume, 7×10^{-9} mgm. deoxyribonucleic acid/cell—corresponding to $0 \cdot 6 \times 10^{-8}$ µmol. thymidine/cell. Since the circulating cells represent only a portion of the total body leucocytes, the extent of incorporation into the latter is estimated at several times the 1 per cent value calculated for the former.

Hamilton has used radiocarbon-labelled precursors of nucleic acid bases to study nucleic acid turnover in human leukæmic cells[9,10]. Since labelled 5-iododeoxyuridine is an analogue of thymidine, its incorporation into leucocyte deoxyribonucleic acid as a function of time after administration may also yield useful information concerning nucleic acid metabolism. The short half-life (8·0 days) of iodine-131 relative to radiocarbon and tritium may be of advantage in certain studies in the human.

In an attempt to evaluate differential energy absorption in white blood cells as compared with whole blood, the iodine-131 activity of plasma, red blood cells and white blood cells was determined over a 12-day period. The concentration of iodine-131 in white blood cells was greater than that in red blood cells and plasma during this period with a maximum factor of 40 on the sixth day. By integrating the areas under the curves for each of these fractions, estimates of radiation delivered to packed white blood cells and whole blood were made. The β-radiation for packed white blood cells and whole blood was 0·94 and 0·23 rad/mc. of dose respectively. The γ-radiation affecting the whole body was calculated from the body retention curve, assuming that 40 per cent of the γ-ray energy was absorbed in the body. This added 0·35 rad/mc. In this way, the total radiation absorbed in packed white blood cells was estimated to be 2·2 times that of whole blood. In so far as radiation conditions for packed white blood cells can simulate that for leukæmic infiltrates, this would be a favourable factor in consideration of possible radiotherapeutic applications[11].

Counting at skin-contact was carried out with a scintillation crystal at intervals for two weeks after administration of 5-iododeoxyuridine. The splenic area yielded a higher count than any other. At 6 days the difference between spleen and mid-thigh area was maximal and the organ-thigh ratio was 27 for spleen, 11 for liver, and 6 for cæcum and urinary bladder.

The dependence of the extent of incorporation of iodine-131 into the deoxyribonucleic acid of rapidly proliferating tissues on the mode of 5-iododeoxyuridine administration is under investigation. Measurement of differential energy absorption in a number of tissues

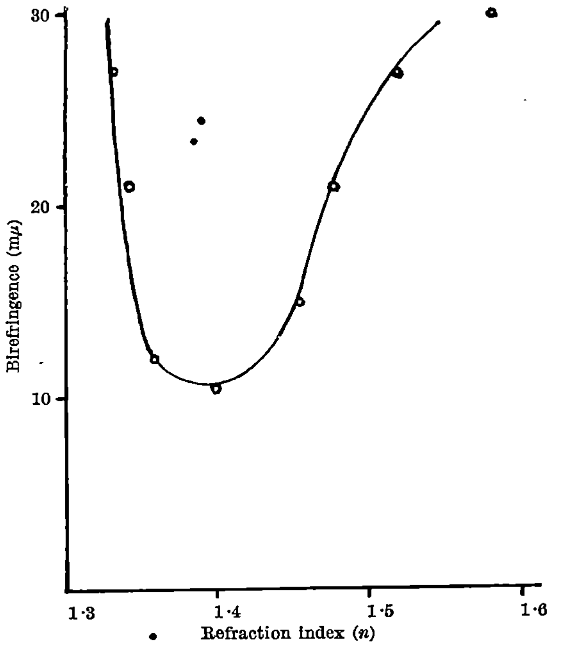

Fig. 2. Birefringence of a single lamella as a function of the refraction index of the embedding medium

curve does not decline to zero even at the point of its minimum ($n = 1{\cdot}4$). This rest (crystalline) birefringence indicates that the intralamellar micelles themselves are birefringent, that is to say, the polypeptide chains are oriented inside the micelles. The positiveness of the rest birefringence proves the longitudinal orientation of these chains.

According to our investigations, the highly specialized function of the postsynaptic membrane is rendered possible by a highly organized and at the same time very labile structure. Details concerning the submicroscopical pattern of other synaptical structures will be reported later.

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5-Hydroxytryptamine in Blood during Experimental Traumatic Shock in Rats

It has been shown that the level of histamine in blood increases very much during experimental traumatic shock in rats[1]. Evidence has been presented that body 5-hydroxytryptamine (5-HT) might be influenced by the same factors as histamine[2–4]. We therefore investigated blood-levels of 5-hydroxytryptamine during experimental traumatic shock in rats.

Adrenalectomized white rats were subject to shock by limb ischæmia[5]. Rubber tourniquets were applied on both hind legs for 2 hr.; 45 min. later, when the signs of the shock became evident, the animals were killed and blood samples taken. 5-Hydroxytryptamine was extracted with 4 volumes of acetone for 24 hr. and determined on Vane's isolated rat fundus preparation[6]. The results are shown in Table 1. During shock, the blood-level of 5-hydroxytryptamine was found to be approximately four times as great as the normal value ($P < 0{\cdot}001$). Table 1 shows that the level of 5-hydroxytryptamine in the blood decreased in adrenalectomized control animals as compared with that found in normal rats (for which the values obtained were in good agreement with those found by other authors[7]). This indicates that adrenalectomy might influence blood-levels of 5-hydroxytryptamine.

Table 1. 5-Hydroxytryptamine in Rat Blood

	(1) Controls, normal	(2) Controls, adrenalectomized	(3) Traumatic shock adrenalectomized	P
5-HT (μgm./ml.) (mean ± *S.E.* of the mean)	0·276 ± 0·050	0·095 ± 0·010	0·371 ± 0·052	3 : 2 <0·001

The mechanism by which the level of 5-hydroxytryptamine in blood is raised during traumatic experimental shock is unknown. It is possible that some toxin from the ischæmic limb releases this substance. Hæmoconcentration, which ensues during shock with the increased number of blood platelets, could not significantly influence blood-levels of 5-hydroxytryptamine, since, while hæmoconcentration amounted to 130 per cent, the level of 5-hydroxytryptamine in the blood was increased to 400 per cent.

As to the significance of the elevation of blood-level of 5-hydroxytryptamine during experimental traumatic shock, it should be pointed out that this substance was found to be released from blood platelets during anaphylactic shock in rabbits[8], but the signs of this shock in the guinea pig were found not to be causally related to 5-hydroxytryptamine[9]. On the other hand, evidence exists that the anaphylactoid reaction in rats is mediated chiefly through the release of 5-hydroxytryptamine[10,11]. It is not possible as yet to say whether the increase of 5-hydroxytryptamine in the blood which occurs during experimental traumatic shock is causally related to the appearance of signs of this condition. However, it should be noted in this connexion that 5-hydroxytryptamine was found, like histamine, to increase the permeability of blood vessels[3,4].

The mechanism and the possible causal relation between the elevation of 5-hydroxytryptamine in the blood and the signs of the experimental traumatic shock are being investigated further.

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will facilitate appraisal of any potential radiotherapeutic use for labelled 5-iododeoxyuridine administration.

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Temperature Control of Physiological Dwarfing in Peach Seedlings

One of the key problems in germination physiology is the mechanism of embryo 'dormancy' or rest. One aspect of this problem is the physiological dwarfing which has been reported to occur in the seedlings of woody plants, especially of such commercial fruits as peaches. These seeds normally require an extended period of low-temperature after-ripening to permit germination. However, if the seed-coat is removed from non-after-ripened seeds germination occurs, but the shoots of such plants are abnormal with telescoped internodes and leaves which may be deformed or sometimes reduced to a rosette of white, scale-like appendages[1,2]; the exact symptoms are a varietal characteristic[3]. Low-temperature after-ripening of the seed or seedling is commonly reported to be essential to produce a normal plant.

The symptoms of physiological dwarfing in seedlings are similar to those shown by buds of trees forced after insufficient chilling. Several authors have therefore suggested[1,4,5] that the mechanisms of physiological dwarfing and the rest period in buds may be the same. In view of this similarity, and a growing body of evidence that the rest period is the result of the action of chemical inhibitors[6], several anomalous features of this phenomenon should be recognized. In the first place, dwarf seedlings have been reported to remain growing but dwarfed for as long as ten years[2], a period inconsistent with the known stability of compounds in biological systems. Secondly, the dwarfing symptoms are restricted to the leaves and stem produced directly by the epicotyl apex[1,3]; branches formed are always normal. Such precise anatomical localization is difficult to correlate with an inhibitor molecule of sufficiently small size to be chromatographed and detected in an auxin analysis system.

Table 1. Effect of Germination Temperature on the Development of Dwarfing Symptoms in Elberta Peach Seedlings from Non-after-ripened Seeds

	Germination in light			Germination in dark		
	19° C.	23° C.	27° C.	19° C.	23° C.	27° C.
Average height (cm.)	17·4	16·8	15·7	17·7	17·7	15·0
Average number of nodes per plant	18·5	16·8	15·2	17·4	18·9	14·6
Average number of nodes with abnormal leaves	0	0·8	5·5	0·7	1·7	7·1
Relative severity of dwarfing (0–4)	0	0·3	2·2	0·6	0·9	3·7

Recently we have discovered a third anomaly: physiological dwarfing is not an obligatory state in the development of a seedling from a non-after-ripened seed. Such seedlings may be either dwarf or normal; the expression, or failure thereof, of the dwarfing character is a function of the temperature to which the seed is exposed during the first few days of germination. The temperature-range for this effect is extremely small, approximately 4° C., and lies within the range of 'normal' germination temperatures.

Results of a typical experiment showing this temperature effect are presented in Table 1. In this experiment, seeds of *Prunus persica* Sieb. and Zucc. var. Elberta were sterilized by immersion for 10 min. in a 5 per cent suspension of 'Pittchlor' (Columbia, Southern Chemical Corp.), rinsed, and allowed to imbibe in the dark at 25° C. for 24 hr. The seed-coat and endosperm for about one-third the length of the seed at the hypocotyl end were excised aseptically and the seeds germinated, approximately ten in a 15-cm. Petri dish. Three germination temperatures were used. At each temperature one dish was exposed to continuous illumination 70 cm. from 40-watt standard cool white fluorescent tubes on 2-in. centres with 20 per cent added incandescent wattage. A dark control at each temperature was obtained by wrapping a dish in black polyethylene. To distinguish between light and temperature effects, the dishes rested in stainless steel trays immersed in constant-temperature water baths adjusted to give the desired seed temperature. This was necessary since high-intensity fluorescent lights produce sufficient heat to raise the level at the germinating surface considerably above ambient temperature unless special precautions are taken. After germination for seven days, the seedlings were planted in coarse white sand, watered daily with a mineral nutrient solution, and grown under the fluorescent lights described above on a 16-hr. day with day temperature of 27° C. and night temperature of 22° C. After a growing period of 5 weeks the height of the plants was measured and the total number of nodes counted, including nodes with scale leaves (germination in peach is hypogeal). In Elberta peaches grown under these conditions, dwarfing is primarily shown by distorted leaves which are abnormally wide but short and twisted as a result of the failure of midrib elongation. Severity of dwarfing was scored in two ways: (1) on an arbitrary scale of 0–4 based on a visual estimate of degree of abnormality; (2) by counting the number of nodes with abnormal leaves.

From the results, it is clear that there is little if any difference between seedlings germinated in the light and those germinated in the dark. Germination at the higher temperatures results in a slight reduction in height of plant and number of nodes. The major effect of temperature is on the development of dwarfing symptoms. At 19° C. all plants were essentially normal; at 27° C. they were all severely dwarfed. At 23° C. only a few plants showed dwarfing symptoms and few of these were severe. Thus the effective range for the development of dwarfing symptoms is approximately 4 deg. C., between 23° and 27° C. The effective time lies within approximately the first week of germination, since subsequent growth of all plants was at the same temperature.

Thus far we have observed this response in only one peach variety; it is essential to determine whether it is of general occurrence. If dwarfing is temperature-controlled in a number of varieties and species, then immediate practical applications to fruit tree breeding will be possible. The major importance of this observation, however, may lie in suggesting possible new explanations for the mechanism of the rest period. We are therefore continuing the investigation.

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PATHOLOGY

Changes in Specificity and Electrophoretic Mobility of the Precipitating Antibodies present in the Serum of Cattle recovering from Foot-and-Mouth Disease

Graves[1] has shown by agar gel diffusion tests that quantitative differences exist among three different field samples (Channel Island, Ven. 1 and *M*.11) belonging to the same immunological type (Vallée O) of foot-and-mouth disease virus. He noticed, however, that these sub-type differences could not be clearly shown when early convalescent cattle serum (7–14 days) was used for the tests. This was due to the almost equal reaction of the immune serum with the heterologous as well as the homologous virus sub-type. During an examination of the nature of this cross-reaction by immunoelectrophoresis some interesting observations have been made regarding the mobility of the antibodies present in the sera during early convalescence. Cattle sera collected 7, 14 and 21 days after infection with the Channel Island sub-type of the virus were separated electrophoretically in agar by the method of Williams and Grabar[2]. The separated serum proteins were then allowed to diffuse towards the homologous Channel Island virus on one side or the heterologous sub-type *M*.11 on the other. The 7-day convalescent serum gave a precipitin line with both sub-types of the virus whereas the 14 and 21 days sera precipitated only with the homologous Channel Island virus (Fig. 1). In addition to this cross-reaction it was observed that the precipitin lines formed by the 14 and 21 days sera were longer and nearer to the cathode than those formed by the 7 day serum.

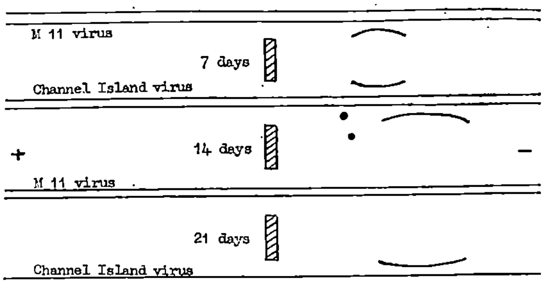

Fig. 1. Immunoelectrophoresis of convalescent sera taken 7, 14 and 21 days after infection with the Channel Island strain of the virus

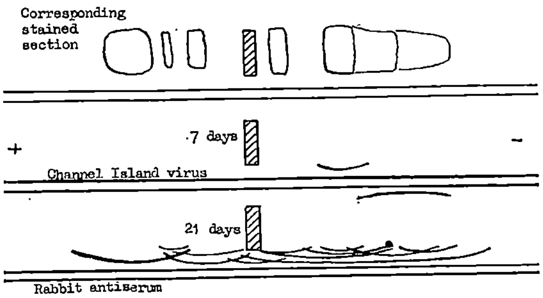

Fig. 2. Immunoelectrophoresis of convalescent sera from cattle after infection with the Channel Island strain of the virus. The positions of the precipitin bands obtained by diffusing the separated proteins towards the homologous virus and rabbit antiserum are compared

In view of this marked difference in mobility it appeared of interest to examine further the nature of the antibodies. The 7 and 21 days sera, following electrophoresis in agar, were allowed to diffuse towards rabbit anti-bovine serum and the positions of the precipitin bands compared with those obtained by diffusion towards the homologous virus. The results of such an experiment are shown in Fig. 2. It appears, on this evidence, that the precipitating antibody present in the 7-day convalescent serum corresponds to a β-type globulin. The precipitin bands obtained when the 7 and 21 days sera are allowed to diffuse from adjacent cups towards the homologous virus do not cross, however, indicating that the antibodies are identical. In addition, a mixture of the 7 and 21 day sera gives one continuous line when examined by immunoelectrophoresis. It may be, therefore, that the antibodies present in both the 7 and 21 days sera are γ-globulins of different electrophoretic mobilities.

Some further evidence has been obtained of the different physical properties of the antibodies present in the two sera. When the 7-days serum, dialysed against 0·01 *M* phosphate *p*H 7·6, is subjected to chromatography on *DEAE*-cellulose in equilibrium with the same buffer solution no virus-neutralizing activity is found in the eluate although complete recovery of this activity can be achieved by elution with 0·05 *M* phosphate *p*H 4·7. On the other hand when the 21-days serum is subjected to chromatography under the same conditions a considerable proportion (more than 50 per cent) of the neutralizing activity initially present in the serum is obtained in the 0·01 *M* phosphate fraction. It is evident that differences exist in the antibodies present in the two sera and these differences are being examined in more detail.

We wish to thank Dr. P. Grabar for his interest in this work and Mr. B. Cartwright for carrying out the serum fractionations.

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Response of Newly Born Mice to a Chemical Carcinogen

Many recent reports record that certain leukæmias and malignant lymphomas can be transmitted to newly born mice using cell-free extracts of tumour tissues[1,2]. Under certain conditions, cell-free extracts of leukæmic organs also produced parotid gland tumours, sarcomas and other neoplasms[3-5]. Tissue culture extracts and extracts of tumour tissues[6-10] have given rise to leukæmias and other tumours in rats and hamsters, following injection into the newly born animal.

Since all these studies have made use of newly born animals, it seemed to us that general studies of the pathological responses of the newly born animals were of considerable importance. We have investigated the effects of certain chemical carcinogens in this same biological system. This communication reports the effects of small doses of the purified carcinogenic hydrocarbon, 9,10-dimethyl-1,2-benzanthracene, administered subcutaneously as a colloidal suspension to newly born Swiss mice. The Swiss mice were originally obtained from the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, and have been bred at random in this laboratory for the past nine years. The incidence of tumours occurring in these animals has been carefully followed in many untreated controls during this time; malignant lymphomas of different types have been found in 4 per cent of animals of more than one year of age but have not been seen prior to this time. A slightly higher incidence of malignant lymphomas (6 per cent) has been noted following a single dose of 9,10-dimethyl-1,2-benzanthracene given by various routes of administration to animals 8–10 weeks old. The earliest lymphomas seen in these animals occurred at 42 weeks of age.

In the present experiment 25 newly born Swiss male and female mice, less than 12 hr. of age, were given a single subcutaneous injection of 30 μgm. 9,10-dimethyl-1,2-benzanthracene as a colloidal suspension. The suspension was prepared by the rapid addition of 9,10-dimethyl-1,2-benzanthracene, dissolved in acetone to 1 per cent aqueous gelatin, kept at 56° C. in a water-bath. The acetone was then removed by slowly bubbling nitrogen through the suspension. Newly born mice were injected subcutaneously in the interscapular region (tuberculin syringe, 26 gauge needle) with 0·015 ml. of the suspension, containing 30 μgm. 9,10-dimethyl-1,2-benzanthracene. The first animal was killed when moribund at the eleventh week from birth and showed a marked enlargement of the thymus which occupied a large part of the chest cavity, compressing the lungs. The spleen and peripheral lymph nodes appeared normal in size and colour. Three more animals were killed when moribund at the thirteenth week; one showed a marked enlargement of the thymus, the lymph nodes and spleen; the other two had an enlarged thymus and multiple lung adenomas less than 1 mm. diameter. Four additional mice, killed at the sixteenth, eighteenth and twenty-fourth weeks, all had enlargement of the thymus, lymph nodes, spleen and multiple lung adenomas. Histologically, these tumours are malignant lymphomas of the stem-cell type with early lymphocytic differentiation. Microscopic infiltrations of lungs, kidneys, skeletal muscles, spleen, lymph nodes, salivary glands and bone marrow were found; but not all these organs were involved in every animal. Thus, eight mice of a group of 25 have developed lymphomas in the short period of 11–24 weeks, at an average age of 15·3 weeks following injection (an incidence of 32 per cent). Control mice were given injections of a similar amount of colloid only; all survive and no tumours have occurred so far.

The finding that polycyclic hydrocarbon carcinogens can give rise to or enhance leukæmia has been reported many times using different strains of mice[11-14]. The present study differs from prior investigations in that only a single, low dose of carcinogen has given rise to a high incidence of malignant lymphoma rapidly in a relatively insusceptible mouse. It is emphasized, from this finding, that the development of this disease is dependent, to a great extent, upon factors inherent to the animals at this stage of development. The character of the response encountered in newly born mice with cell-free filtrates should be viewed not only in terms of virus concepts but also as a response of a sensitive biological system to carcinogenesis.

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Complement Fixation with Tissue Culture and Liver Antigens of Mouse Hepatitis

HOST-SPECIFIC viruses associated with hepatitis of duck[1], dog[2], mouse[3–6], and man[7] have been described. The agents of duck[8], dog[9] and mouse[10,11] hepatitis have been propagated in tissue culture. Complement-fixing antigens have been prepared from infected livers of mouse[12] and dog[13]. However, studies on propagation and serology of human hepatitis viruses have as yet yielded equivocal results[14]. By means of virus-neutralization tests in mice, Gledhill *et al.*[15] noted an antigenic relationship among strains of murine hepatitis virus. They stated that *JHM*, Nelson, and *MHV* strains probably form a related group of viruses.

This report describes a complement-fixation test with liver antigens in which a relationship was noted between Gledhill's[16] *MHV*-1 and Nelson's[17] *PRI* mouse hepatitis strains. In addition, complement-fixing antigen was demonstrated in serially passaged tissue cultures of *MHV*-1. Tissue cultures showed no definite cytopathogenic effect but were infective for newly born mice.

The complement-fixing procedure used was essentially that described by Bengtson[18]: 0·2 ml. quantities each of antigen dilutions, serum (inactivated as a 1 : 10 dilution in saline at 61° C. for 20 min.), and complement (2 units) were used; after incubation overnight at 4° C., the hæmolytic system was added; complement fixation was determined visually after subsequent incubation at 37° C. for 30 min.

Complement-fixing antigens were prepared from liver homogenates of suckling mice infected with *MHV*-1 and of weanling mice (8–10 gm.) infected with *PRI* virus. Whole cultures of serially passaged *MHV*-1 in mouse kidney explants[11] were also used as complement-fixing antigens. Later experiments indicated that nutrient fluids alone contained this complement-fixing antigen. Control antigens were prepared from liver homogenates of normal weanling and suckling mice and from uninoculated tissue cultures. Each antigen preparation was centrifuged at 40,000*g* for 1 hr. at 4° C. to eliminate sedimentable non-specific complement-fixing factors which occurred occasionally with some pools of control material centrifuged at lower speeds.

Tissue culture and liver preparations containing *MHV*-1 were assayed for infectivity in newly born Swiss mice[11]. Titres of 8 different *MHV*-1 liver pools had *ID*50 end-points of $10^{-3\cdot 0}$ to $10^{-3\cdot 5}$/0·05 ml. of inoculum. Ten serially passaged tissue cultures of *MHV*-1 yielded ID50 end-points from $10^{-4\cdot 1}$ to $10^{-5\cdot 2}$ (Table 2). The *PRI* liver homogenates had *ID*50 end-points from $10^{-3\cdot 2}$ to $10^{-3\cdot 6}$/0·1 ml. inoculum when assayed in weanling Swiss mice (8–10 gm.).

Table 2. COMPARISON OF INFECTIVITY AND COMPLEMENT-FIXATION TITRES OF SERIALLY PASSAGED TISSUE CULTURES OF *MHV*-1

Passage No.	Dilution of original virus	Infectivity titre* −log *ID*50		Complement-fixing titre reciprocal of antigen dilution			
		0 hr.	96 hr.	0	2	4	8
1	10^{1}	2·4	4·8	*NT*†	*NT*	*NT*	*NT*
2	10^{3}	3·0	4·6	*NT*	*NT*	*NT*	*NT*
3	10^{4}	2·5	4·8	++++	+++	−	−
4	10^{5}	3·8	5·2	++++	++++	−	−
5	10^{7}	1·9	4·4	+	−	−	−
6	10^{8}	*NT*	4·7	++++	+++	−	−
7	10^{9}	3·7	4·1	++++	++++	++++	−
8	10^{10}	3·5	4·8	++++	−	−	−
9	10^{11}	3·6	4·2	*NT*	++++	++++	−
10	10^{12}	2·7	4·3	++++	++++	−	−

* See ref. 11. † Not tested.

Antisera were prepared in adult Swiss mice by intramulscular injection of extracts of either normal or infected mouse liver. Inocula were combined with adjuvant (mineral oil/'Arlacel'/antigen, 1·0 ml. : 0·1 ml. : 1·0 ml., respectively) and two injections of 0·2 ml. each of the mixture were given 14 days apart. Groups of 40–60 immunized mice were bled 14 days later and their sera were pooled. Control sera were obtained from untreated mice.

Results of box titration tests showed cross complement-fixing reactions between *MHV*-1 and *PRI* virus (Table 1). Normal liver antigen did not fix complement in the lowest dilutions of serum and antigen tested. However, 1 out of 10 supposedly 'normal' serum pools fixed complement in the presence of *MHV*-1 and of *PRI* liver preparations. As viral agents causing hepatitis in mice have appeared 'spontaneously' during the course of studies on enteric disease of the suckling mouse[6], human viral hepatitis[3,19] and mouse leukæmia[5,17], it is possible that some donors to this positive 'normal' serum pool had in fact been infected with a murine hepatitis virus related to *MHV*-1 or *PRI*.

Antigens processed from *MHV*-1-infected, kidney explant tissue cultures fixed complement in the presence of *MHV*-1 immune serum (Table 2). All serum pools were diluted 1 : 10 in saline and inactivated (61° C. for 20 min.) prior to use. Control serums and antigens were negative in this system. It appears that complement-fixing titres obtained with tissue-culture antigens were somewhat lower than those obtained with liver antigens. Of 18 additional mouse-kidney tissue-culture antigens tested, infectivity titres ranged from *ID*50 $10^{-1\cdot 9}$ to $10^{-5\cdot 2}$ and complement-fixing titres from 1 : 0 to 1 : 8. A relation-

Table 1. CROSS-REACTIONS BETWEEN COMPLEMENT-FIXING ANTIGENS OF *MHV*-1 AND *PRI* MOUSE HEPATITIS VIRUSES

			Liver antigen – reciprocal of dilution									
			MHV-1					*PRI*				
			4	8	12	16	20	4	8	12	16	20
Immune serum – reciprocal of dilution	*MHV*–1	10	++++	++++	++++	++++	+	++++	++++	++++	++	−
		20	++++	++++	+++	++	−	++++	++++	++++	−	−
		40	++++	++++	++	−	−	++++	++++	+++	−	−
		60	++++	++	−	−	−	++++	++++	+	−	−
		80	++++	−	−	−	−	++++	++++	−	−	−
	PRI	10	++++	+++	−	−	−	++++	++++	+	−	−
		20	+++	−	−	−	−	++++	+++	−	−	−
		40	++	−	−	−	−	++++	++	−	−	−
		60	+	−	−	−	−	++++	+	−	−	−
		80	−	−	−	−	−	++++	+	−	−	−

ship was not noted between complement-fixing and infectivity titres in these tests.

A relationship was demonstrated between the *MHV*-1 and *PRI* murine hepatitis strains by complement-fixation tests. Specific antigen was obtained from serially passaged, *MHV*-1-infected, mouse-kidney tissue cultures which fixed complement in the presence of immune serum prepared in mice with extracts of *MHV*-1-infected liver in adjuvant.

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Incorporation of Thymidine labelled with Tritium by Circulating Cells of Infectious Mononucleosis

CONSIDERABLE uncertainty exists about the origin and the identity of the cells of infectious mononucleosis. They have been described as atypical lymphocytes, as monocytes, as reticular-endothelial cells developing towards a lymphomonocyte or even a plasma cell. Most hæmatologists[1,2], however, regard them as mature cells, even though they do vary greatly in size and shape.

Useful information on this subject could certainly be obtained by a functional study of these cells. Autoradiography provides a powerful tool for investigation at a cellular level. Moreover, the availability of compounds labelled with tritium has greatly improved the resolution of this method. Thymidine-^{3}H is known to be a specific precursor of deoxyribonucleic acid; therefore, its incorporation into cell deoxyribonucleic acid is evidence of active deoxyribonucleic acid synthesis, possibly preparatory to later mitosis.

Incorporation of thymidine-^{3}H has been investigated in the peripheral blood of three cases of infectious mononucleosis and of two normal subjects. In infectious mononucleosis incorporation has been followed during the various stages of the disease up to complete recovery. All cases showed a complete clinical picture, a characteristic hæmatological pattern and a highly positive Paul–Bunnel test.

Blood was withdrawn from the antecubital vein and 2 ml. of a 5 per cent dextran solution (molecular weight 150,000) was added to 8 ml. of citrated blood. After 20 min. the supernatant was pipetted into a test-tube; the white cells were washed twice in normal saline with low-speed centrifugation and then resuspended in Eagle's medium. This procedure was carried out under sterile conditions. Thymidine-^{3}H with a specific activity of 390 mc./mM was then added to a final dilution of 5 μc./ml. Incubations were in a water-bath at 37° C.; samples of cells were withdrawn after 2, 4 and 6 hr. and smears were made on gelatin-coated slides. The smears were fixed in Carnoy's solution, and, after several washings in distilled water, stripping films (Kodak *AR*-10) were placed over the slides according to the method described by Pelc[3]. The films were developed after ten days exposure and smears stained through the stripping film with May–Grünwald–Giemsa. For each slide 4,000 cells were counted to determine the amount of labelling.

The percentage of labelled cells detected in normal individuals corresponded strictly to that observed by Bond *et al.*[4], that is, 0·06 per cent referred to the number of total white cells; labelled cells were all large lymphocytes or monocytes. In cells from patients affected by infectious mononucleosis considerably higher values were observed (Table 1); in the first stage of the disease, for example, the mean percentage of labelled cells, after 2 hr. incubation, was 4·44, that is, more than thirty times the value for normal blood. This percentage decreased progressively during the course of the disease and, with the complete recovery, reached the normal value. In the first stage of the disease only the percentage of labelled cells increased linearly with the time of incubation, from 4·44 (second hour) to 10·5 per cent (sixth hour). This linearity was no longer detectable in the later stages.

Table 1. PERCENTAGE OF LABELLED LYMPHOMONOCYTES AT DIFFERENT STAGES OF THE DISEASE (AFTER 2-HR. INCUBATION)

Stage	Cases			Mean value	σ ±
	1	2	3		
1	3·8	4·3	5·2	4·44	0·57
2	1·1	2·1	1·4	1·53	0·41
3	0·30	0·30	0·15	0·25	0·12
4	0·066	0·075	0·048	0·063	0·011

Stages: 1, Acute phase of the disease; 2, early improvement; 3, full improvement; 4, complete recovery.

Our results clearly show that in infectious mononucleosis the cells of the peripheral blood have a greater tendency to synthesize deoxyribonucleic acid than normal lymphomonocytes. This synthesis may be preparatory to subsequent mitosis, though this cannot be considered as direct evidence of mitosis. No mitotic figures were observed in any of the slides we examined. Mitosis in the peripheral blood of infectious mononucleosis patients has been only occasionally reported[5-7].

The incorporation of deoxyribonucleic acid precursors by bone marrow cells has been used to calculate the mitotic cycle of these cells[8]; in our case, however, the degree of incorporation during the period of incubation does not permit such a study because it is not certain that all mononuclear cells of the peripheral blood will undergo mitosis; moreover, as demonstrated by Painter[9], the radiobiological effect of thymidine-^{3}H incorporated in the chromosomes may, in *in vitro* experiments, affect the proliferative activity of the cells.

The most important fact shown by this investigation is that the cells of infectious mononucleosis behave in a completely different way from the lymphomonocytes of normal peripheral blood with respect to deoxyribonucleic acid synthesis. It is therefore reasonable to consider them as totipotent cells of mesenchymal origin, which actively proliferate in the organs and easily enter the peripheral blood. As an alternative hypothesis one might suggest that the increased synthesis of deoxyribonucleic acid may indicate virus synthesis within the cells.

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BACTERIOLOGY

Measurement of a Staphylococcal Antibody in Human Serum by a Mouse Protection Test

THE need for a better understanding of immune phenomena related to staphylococcal infections has been repeatedly emphasized[1]. In so far as humoral antibodies are concerned, a substantial amount of work has been done only with staphylococcal antitoxins. However, as pointed out by Rountree and Barbour[2], this approach has not appeared to be rewarding. It has also been suggested that anticoagulase may be an important antibody[3]; but some doubt exists as to the significance of coagulase in staphylococcal infections[4,5]. Although a promising serological procedure was developed by Rountree and Barbour[2], this method was not applied in a study of infections.

It has been postulated that one of the most significant tests of the importance of antibody is the demonstration of its protective activity in experimentally infected animals[6]. Therefore, the application of the mouse protection test described in this communication may provide a useful new approach for the study of staphylococcal immunity. In addition this procedure not only provides acceptable sensitivity but can also be used to measure the staphylococca antibody content of a given serum.

Since the mechanism of action is at present unknown for this antibody, it is described functionally as 'mouse protective antibody'. The specificity o mouse protective antibody has been established by absorption procedures, similar to those used for determining antibody specificity in human gamma globulin[7], and will be reported elsewhere. Its 'classic antibody nature is also supported by the fact that mouse protective antibody potency was unaltered by exposure to 60° C. as long as 4 hr.

In performing a mouse protective antibody assay 18–22 gm. albino Webster mice, either sex, are injected intraperitoneally with 10–20 *LD*50 of the Smith strain of *Staphylococcus aureus*. This inoculum consisting of about 10^4 cells, is derived from a 12–18 hr broth culture and is suspended in 5 per cent hog gastric mucin, using 0·5 ml./mouse. As described by Hunt and Moses[8], this dose of Smith staphylococcus will produce an acute systemic infection, lethal to 90–100 per cent of untreated mice within 24 hr Although most of these studies have involved the Smith strain, comparable activities of given serum have been obtained with other staphylococcal strains

Within 30 min. of challenge, groups of mice ar injected intraperitoneally with 0·25 ml. each o varying saline dilutions of the serum to be titrated A preliminary test is performed first with 40 mice 10 untreated controls and three groups of 10, using serum dilutions of 1 : 10, 1 : 100 and 1 : 1,000. Th five-day survival values obtained from this test ar used as a guide for setting up a definitive titration In the second assay, groups of 15–20 mice and two fold serum dilutions are employed. Usually, fou serum dilutions will suffice for obtaining surviva data ranging between 0 and 100 per cent, so that minimum total of 115 mice is required for the preliminary and definitive assays. As indicated, a five day observation period will provide final surviva results, and, in general, no more than 2 ml. of serum are required for the entire assay.

A typical set of results is given in Table 1 for given serum, illustrating the preliminary and definitive assays and the increasing protective activity (increasing amounts of serum. The survival percentages derived from the definitive assay ar employed for the estimation of mouse protectiv antibody titre, which can be expressed as the 50 pe cent protective dilution (*PD*50). A practicable mea of determining the *PD*50 with such survival data the Miller–Tainter method[9]. The *PD*50 derived fro the results shown in Table 1 is given at the botto of the table.

Table 1. REPRESENTATIVE RESULTS OF MOUSE PROTECTION TEST, PRELIMINARY AND DEFINITIVE, OF A HUMAN SERUM SPECIME

Serum dilution	Survivors/total	Survivors (per cent)
Preliminary:		
None (untreated)	0/10	0
1 : 10	10/10	100
1 : 100	9/10	90
1 : 1,000	1/10	10
Definitive:		
None (untreated)	1/20	5
1 : 100	19/20	95
1 : 200	16/20	80
1 : 400	8/20	40
1 : 800	3/20	15

50 per cent protective dilution, 1 : 350

Analyses of 50 sera from normal adults revealed *PD*50 titres ranging between 1 : 3 and 1 : 2,000. The geometric mean titre of this group was 1 : 192, as calculated by Perkins's method[10]. Limited studies have shown that persons with a chronic staphylococcal infection, furunculosis, had serum *PD*50 titres in the low range : 1 : 10 to 1 : 60. It has also been noted that, out of 54 pairs of maternal and newly born (cord) sera, 41 exhibited comparable mouse protective antibody, but 13 cord sera were substantially lower in mouse protective antibody content than were the respective mothers. This observation suggests, as noted by Rountree and Barbour[2], that in some instances there may be a placental barrier to the transmission of staphylococcal antibody to the fœtus. Studies are in progress to determine the incidence of staphylococcal infection among the newly born and their mothers with respect to their mouse protective antibody titres.

The widespread occurrence of staphylococcal mouse protective antibody in adult human sera indicates that this is a normal antibody, a characterization that was previously applied by me for staphylococcal and other bacterial mouse protective antibody in pooled human gamma globulin[11]. This conclusion has been recently substantiated by Jensen[12], who employed a qualitative agar gel precipitin method for demonstrating staphylococcal antibody in human sera.

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Immunizing Properties of Insoluble Cell Material derived from *Brucella*

AN insoluble fraction was obtained by high-speed centrifugation from *Brucella suis*, after disintegration in a sonic vibrator[1]. This fraction could absorb the agglutinating and mouse protecting antibodies from *B. suis* antisera. Since similar absorptions could be carried out, although less effectively, with whole bacteria, the insoluble material was assumed to be situated on the cellular surface and tentatively regarded as part of the cell wall.

The present work was concerned with the immunizing properties of two insoluble fractions derived from *B. abortus* and *B. suis*. The starting material consisted of bacteria killed and dried with acetone, disintegrated in a 9-kc./s. Raytheon magneto-striction oscillator. The sonic extract was centrifuged in a Sorval centrifuge at 10,000 r.p.m. and the sediment freed from intact cells by differential centrifugation. Fraction 1 (*F*1) was thus obtained. Fraction 2 (*F*2) consisted of smaller particles sedimented from the supernatant fluid left from the first centrifugation, after spinning for 30 min. in a Spinco model *L* ultracentrifuge at 40,000 r.p.m. The immunizing activity of these fractions was compared in mice with that of whole cells killed and dried with acetone, following a method previously used in passive protection experiments[2]. 0·01–1 mgm. quantities were injected intra-abdominally into groups of 5–10 mice. At various times after immunization (2–14 weeks) the immune animals were challenged, together with controls, with 30,000 virulent *B. abortus* (strain 2308) cells administered intra-abdominally. 7 days later the mice were killed with ether, the spleens removed, ground with glass sand and plated on trypticase soy agar. Protection indices were calculated as the ratio of the number of *Brucellae* in the spleens of normal mice to that in the spleens of the immune mice. Higher indices were consistently obtained with the insoluble fractions and the small particle fraction (*F*2) appeared to be more effective than *F*1 (Table 1).

Table 1. IMMUNIZING ACTIVITY OF WHOLE, DRIED *Brucella* CELLS AND OF INSOLUBLE FRACTIONS DERIVED FROM THEM

Immunizing antigen	Protection indices when challenge given at weeks after immunization 2	3	6	12	14
B. abortus whole cells	270	–	30	—	8*
B. abortus Fraction 1	541	—	750	—	53*
B. suis whole cells	25	—	—	—	—
B. suis Fraction 1	222	236	—	50	—
B. suis Fraction 2	—	3,535	—	600	—

One immunizing injection was administered. Groups marked with an asterisk received 1 mgm. antigen, the others received 0·1 mgm.
—, Not done.

The higher efficiency of the insoluble fractions, as compared with whole bacteria, was evident in many other experiments not reported here.

It appears very likely, in view of their serological properties, that the insoluble fractions are cell-wall fragments of various sizes, as already stated in a previous publication[1]. Chemical and spectrophotometric determinations are in progress to confirm this assumption. Although little studied so far[3], cell-wall material has already been found a good immunizing antigen[4,5], and the present work shows it to be of promise in immunization against *Brucella*. Recent work[6,7] suggests, however, that some of the activity shown by the cell wall may be non-specific. Experiments are under way to determine to what extent the effects described above might be reproduced with non-related cell-wall material.

This is a preliminary report on an investigation carried out by one of us (J. M.) in partial fulfilment of the requirements for the Ph.D. degree of the Hebrew University—Hadassah Medical School.

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BIOLOGY

Atmospheric Pollen in Relation to Land Use

THAT the present provides the key to the past is a geological commonplace, and considerable attention has been paid accordingly to the interpretation of pollen diagrams in the light of pollen analyses of recent or surface samples[1,2]. Formerly such investigations centred mainly on the composition of a fossil pollen spectrum as a reflex of its contemporary tree flora. To-day interest, more particularly in western Europe and especially in Britain, has widened to include not merely the composition of forests in prehistoric and early historic time but also the extent and character of the vegetation which, as the result of human activity or of other causes, has more and more replaced forest. A consideration of the composition of to-day's pollen rain in relation to present land use has therefore become desirable.

In the course of an atmospheric pollen census begun in 1942, and still continuing[3], pollen spectra have been obtained from some fifteen centres in Great Britain; but most of them are from inland localities in the lowlands and therefore so heavily weighted with local pollen as to be of little use as reflexes of regional (as opposed to strictly local) land use. Two complete and continuous sets of daily analyses have, however, been made for five years (1945–49) in each of two high, remote and virtually treeless localities among the Brecknockshire mountains, namely, one at Storey Arms on the Beacons road (1,400 ft.) between Merthyr Tydfil and Brecon and the other at Grwyne Fawr Reservoir (1,600 ft.) in the heart of the Black Mountains. A summary of the results of the two sets of analyses is set out in Table 1. The figures in the column headed T.T.P. (total tree pollen) indicate the total numbers of the pollen grains usually included by palæopalynologists under the heading of total tree pollen, namely, birch, pine, elm, oak, lime, alder, beech, hornbeam and ash; those in the columns headed N.T.P. (non-tree pollen) include all herbaceous pollens; other arboreal pollens than those under T.T.P., and all damaged and unidentified grains have been omitted, and the relation between N.T.P. and T.T.P. is seen to be much the same at both stations.

The kinds of pollen (listed above) that make up the T.T.P. are produced by broad-leaved woodlands and pine plantations together, while those that form the N.T.P. come very largely from cultivated land, though some (probably a relatively small proportion) come from the large area recognized as rough grazings (here almost all heavily grazed mountain land). The relevant figures for the respective types of land use have been extracted from the Forestry Commissions Census Reports[4,5] allowance being made for small woods and hedgerow trees[6] and the Ministry of Agriculture's Agricultural Statistics 1945–49 [7], respectively, and are set out in Table 2 first for Brecknockshire alone and then (since some of the pollen trapped must have come from outside that county) for Brecknockshire and five adjacent counties together (Cardiganshire being omitted as too remote).

Table 1. POLLEN DEPOSITION ON BRECKNOCKSHIRE MOUNTAINS, 1945–49

(Grains caught and identified on 5 sq. cm. of horizontal surface)

Station	Total tree pollen (T.T.P.)	Non-tree pollen (N.T.P.)	N.T.P. as percentage of T.T.P.
Grwyne Fawr (Black Mountains)	7,594	22,652	297
Storey Arms (Brecon Beacons)	9,046	27,798	310
Two stations together	16,640	50,450	303

In Table 2 the area entered as arable includes rotation grasses: rather more than one-third of this grassland, taken together with the 'permanent grass', was mown in 1947. It will be seen that whereas N.T.P. on the Brecknockshire mountains is about 300 per cent of T.T.P. (Table 1), the corresponding area of cultivation ('crops and grass') is between 420 and 630 per cent, or, say, 500 per cent, while the area of cultivated land and rough grazings together is between 1,120 and 970, or, say, 1,000 per cent, that of pollen productive woodland. Hence the pollen productivity (in T.T.P.) per unit area of woodland, as measured by pollen precipitation in an area partly fringed (at a distance here averaging 5 miles) by woods, must lie between 5/3 and 10/3 times (that is, between 166 and 333 per cent) of the pollen productivity (in N.T.P.) per unit area of non-forest land lying around the same periphery. Whether the lower or the higher figure is more nearly correct must depend on the pollen productivity of the rough grazings which immediately surround both stations and which, to judge from their botanical composition and the heavy grazing to which they are subjected, must in general be low.

The composition of the pollen rain at these two stations has been worked out in some detail. Thus, grass pollen on the Brecknockshire mountains makes up four-fifths of the N.T.P., that is, it is equivalent to say 250 per cent of the T.T.P. Dr. Verona Conway[8], in her studies of Pennine blanket peats at altitudes varying from 1,200 to 2,050 ft., recorded, in her Zone VIII (modern), grass pollen values of 15–300 per cent of T.T.P., and obtained also from surface blocks values up to 300 per cent. Having regard to the much greater disparity at present existing between woods on one hand and crops, grass and rough grazings on the other in Derbyshire (from which county most of the pollen precipitated on the southern Pennines is derived) as compared with South Wales, a much higher grass pollen figure than 300 per cent might be expected in the former area to-day. It seems likely, therefore, that, provided differential pollen destruction during fossilization can be excluded, Dr. Conway's highest figures relate to a time when deforestation was much less widespread than it is now.

Table 2. LAND USE IN AND AROUND BRECKNOCKSHIRE (ACRES)

	Woodlands productive of T.T.P.	Crops and grass				Rough grazings	Crops, grass and rough grazings together		Total land area
		Arable including rotation grasses	Permanent grass	Total	As percentage of woodlands		Total	As percentage of woodlands	
Brecknockshire	36,000	69,349	82,011	151,360	420	251,698	403,058	1,120	466,347
Six counties	238,000	646,473	860,078	1,506,551	630	798,260	2,304,811	970	2,751,772

Again, pollen of ribwort plantain (*Plantago lanceolata*, an almost invariable concomitant of agriculture from Neolithic times onwards)[9] plays an important part in analyses of pollen to-day. It is, next to grass and nettle pollen, the largest constituent of the N.T.P. precipitated on the Brecknockshire mountains, giving values (in terms of T.T.P.) of 10·6 per cent at Storey Arms, 13·2 per cent at Grwyne Fawr, and an average of 12·2 per cent for the two taken together. Godwin[10] obtained similar counts of plantain pollen (up to 10 per cent of T.T.P.) from Neolithic or post-Neolithic lake deposits on the edge of the East Anglian Breckland; the same author's analyses of peat datable between the Middle Iron Age and the middle of the Roman period in Somerset[11] gave much higher values (up to 60 per cent of T.T.P.). Since deforestation and the spread of agriculture can scarcely have been more general in Somerset around A.D. 0 that it is in South Wales to-day, the figures last quoted would seem to be due to quite local influences.

It is hoped to publish the results of this research more fully elsewhere. This work received generous aid in the form of Government grants voted by the Royal Society.

H. A. HYDE

Department of Botany,
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Detachment of Conidia by Cloud Droplets

IT has been found by experiment that conidia may be detached from conidiophores by the impact of minute water droplets in a moving mist or cloud. A preliminary report of this is given since it appears to be a mechanism of spore detachment which has not yet been described.

In an initial experiment, an open Petri dish of nutrient agar was held behind a culture of *Verticillium albo-atrum*, and the colony sprayed with water droplets from a simple atomizer so that some of the droplets swept the colony and were impacted on to the surface of the agar in the dish beyond. The dish was then covered with a lid and incubated. When examined, a number of *Verticillium* colonies were found among the numerous common air-borne mould fungi which developed. No *Verticillium* colonies appeared on control plates when a culture was subjected to puffs of air (with no water droplets) from the same atomizer. Spore detachment was therefore concluded to have been due to the impact of the minute water droplets.

Following this observation, pieces of grass culm and cotton thread soaked in nutrient agar were inoculated with dense spore suspensions of mould fungi and incubated at 100 per cent relative humidity. When the conidiophores were developed, the cultures were placed in air streams into which a continuous stream of water droplets was introduced when required. These droplets were in the size-range 8–210μ diameter with a modal diameter of 78μ.

Table 1. NUMBERS OF SPORES REMOVED FROM *Cladosporium* COLONIES DURING 1-MIN. EXPOSURES TO STREAMS OF AIR AND AIR-CARRYING CLOUD DROPLETS RESPECTIVELY

Colony	Air speed (m.sec.)	Spores detached by air current	Spores detached by air current plus droplets
1	0·5	350	4,800
2	0·7	200	67,000
3	2	250	51,000
4	5	3,000	18,000
5	10	4,000	32,000

In a series of experiments, each colonized stem or thread was supported across the prongs of a simple wire fork and placed before the intake orifice of a Gregory[1] spore trap. An air stream of known velocity was then drawn over the colony for 1 min., and the spores removed sucked on to the sticky surface of the slide in the trap. After changing the trap slide, the air was turned on again for another minute with cloud droplets being simultaneously directed into the stream flowing over the colony so that the conidiophores were bombarded with the water droplets carried by the moving air.

The results for *Cladosporium* are typical, and show that larger numbers of spores are detached by air currents containing minute water droplets than by air currents of the same velocity without droplets.

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New Members of the British Marine Bottom Fauna

A STUDY is being made of the smaller members of the fauna of marine gravels on the sea-bed in the Plymouth area. One aspect of the results so far obtained is concerned with the array of pygmy species encountered, several of which, as might have been expected, are new to the British fauna.

A bucket of shelly gravel from near the entrance to Plymouth Sound below about 7 fathoms of water (collected by Mr. G. R. Forster during an aqua-lung dive) produced three species of Acochlidiacea, a sub-order of Gastropoda not hitherto recognized as British (though all three have been found near Heligoland). These are *Microhedyle lactea* Hertling, *Hedylopsis suecica* Odhner, and *Philinoglossa helgolandica* Hertling. These animals are shell-less and do not exceed 2 mm. in length, and are scarcely detectable if they cannot be examined alive. A specimen of the small holothurian *Leptosynapta minuta* (Becher) was also obtained from this sample: a species not on the British list, but, as I have since been informed by Dr. D. J. Crisp, discovered at Bangor by Dr. B. Swedmark in 1956.

Chief attention, however, has been given to the Eddystone shell gravel, a well-known source of *Amphioxus lanceolatus* (Pallas), and producing a macrofauna, dominated by lamellibranchs, long familiar to workers at Plymouth[1]. The position sampled is between 1 and 2 km. north-west of the Eddystone Rock, some 15 km. from the nearest mainland, and the depth of water above it is 23–28 fathoms.

This gravel also has given *Microhedyle lactea* and *Leptosynapta minuta* in small numbers. One oligochæte worm (not yet determined) and five species of mites of the family Halacaridae have been isolated. Among these mites *Scaptognathus tridens* Trouess. and *Halacarus bisculus* Viets are new to Britain according to Mr. G. O. Evans, of the British Museum (Natural History), to whom I am indebted for checking the identifications.

But the most notable feature of the Eddystone shell gravel is its rich fauna of small crustaceans, as first noticed by Prof. J. E. Harris during an unsuccessful search for young stages of *Amphioxus*. The smaller Malacostraca have been sorted from two separate major samples of gravel (using magnesium sulphate flotation technique), and so far 56 species have been listed. Of these some 20 are new to the Plymouth fauna[2] and five or six are new to science.

The many Amphipoda include a new species of *Metopa* and one of probably a new genus of Syrrhoidae, both among the more numerous species present in both major samples. (Two other new species of special interest are mentioned later.) Tanaidacea proved fairly numerous, dominated by *Typhlotanais microcheles* Sars and *Strongylurella indivisa* Hansen, both species new to Britain and rarely encountered anywhere. Among Isopoda, by far the most frequent have been *Paramunna bilobata* Sars and *Eurycope pygmaea* Sars, both well figured originally[3], but apparently the latter not previously known as British. Of special interest was the occurrence of a single example of *Microjaera anisopoda* Bocquet and Lévi[4], a particularly small blind janirid of 1·2 mm. described recently from two examples taken off Roscoff. Nothing else is known of this genus. More is known of another blind colourless genus, *Microcharon*, which is represented in the gravel by a new species, *M. harrisi* Spooner[5]. Six of the nine species of *Microcharon* so far discovered live in terrestrial ground-water in southern and eastern Europe, and two in coastal sand[6]. It is a genus belonging to the sub-family Microjanirinae, which is a typical element of the interstitial (phreatic) ground fauna, of which the bathynellids were the first to attract attention.

Two other blind 'interstitial' genera have now been found to be represented in the same shell gravel. One is a new genus of the amphipod family Bogidiellidae, so far represented by six species of *Bogidiella* from subterranean fresh water of coastal sand of southern Europe and Brazil. This is the first offshore occurrence of the family. The animal is very fragile, and only one of the fourteen specimens isolated is entire : this one shows a peculiar development of the seventh peræopod.

The remaining discovery is *Ingolfiella*, a genus which for long has stood as a separate sub-order of Amphipoda. Two specimens have so far been found, in a sample of gravel collected on March 30. The six species of this little-known genus show an extraordinary scattered distribution, ranging from the deep water of the North Atlantic (*I. abyssi* Hansen[7]) to caves in the Belgian Congo (*I. leleupi* Ruffo[8,9]). The newly found examples, the first from European seas, differ in small ways from four of the described species, but are clearly very close to *I. acherontis* Karaman from the ground-water of the Macedonian uplands (though presumably will not prove to be identical with it).

The occurrence of three phreatic genera in a marine deposit raises an interesting zoo-geographical issue. Each separately belongs to a taxon of at least sub-family status which is confined to the subsurface domain, and has no normal (that is, eyed and pigmented) representative in the surface waters. These seem to belong to a slow-breeding (and slow spreading) faunistic element which is dispersed through the water held in the rocks and deposits below the lighted surface—not confined to continents, but continuously distributed both through them and under the sea bed. This view supposes that genera arise, disperse gradually in their native medium, and evolve, irrespective of whether air, fresh water, or ocean lie above the strata they inhabit. Any aquatic group, whether marine or fresh water, is a potential ancestor to members of such a fauna.

This idea will be followed up in future work, and the descriptions of new species mentioned above, it is hoped, published in the near future.

G. M. SPOONER

Marine Biological Laboratory,
Plymouth. April 7.

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Early Formation of Sperms in the *ey*^{2} Mutant of *Drosophila*

THE testis of the newly hatched larva of wild-type *Drosophila* contains only spermatogonia which give rise to primary spermatocytes at the beginning of the second larval instar[1,2]. The primary spermatocytes which represent the early prophase of the first meiotic division have bigger nuclei and are larger in size and lie in the posterior end of the testis. This stage in the differentiation of the testis remains unchanged throughout the rest of the larval life. More advanced stages begin to appear after the formation of the puparium, so that 20-hr. old pupæ contain fully mature sperms.

The appearance of sperms in the larval testis has been reported as of rare incidence in the wild type[3]. On the other hand, sperm bundles showed up most frequently in the larval testis of some lethal mutants with prolonged larval life[4]. However, these usually disintegrate and give rise to patches of histolysed germ tissue.

In the present investigations, it has been found that the majority of *ey*^{2} late third instar larvæ, irrespective of the type of the eyeless phenotype which the larvæ will develop, contain stages up to and including sperm bundles. In some specimens, these advanced stages have become degenerate. 3-hr.-old eyeless prepupæ, without any exception, showed fully mature sperms. This shows that *ey*^{2} specimens reach sexual maturity at least 17 hr. before the normal time.

H. H. SHATOURY

Faculty of Science,
Alexandria University,
Egypt.

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FORTHCOMING EVENTS

(*Meetings marked with an asterisk * are open to the public*)

Monday, June 15

Royal Geographical Society (at 1 Kensington Gore, London, S.W.7), at 3 p.m.—Annual General Meeting.

British Society for the Philosophy of Science (in the Joint Staff Common Room, University College, Gower Street, London, W.C.1), at 5.30 p.m.—Dr. D. Bohm : "The Interpretation of Quantum Theory".

Wednesday, June 17

Royal Meteorological Society (at 49 Cromwell Road, London, S.W.7), at 5 p.m.—Mr. E. Knighting : "Numerical Experiments in he Integration of the Meteorological Equations of Motion" ; Mr. J. S. Sawyer : "The Introduction of the Effects of Topography into Methods of Numerical Forecasting".

University College, Department of Philosophy (in the Gustave Tuck Theatre, Gower Street, London, W.C.1), at 5.30 p.m.—Prof. K. Ajdukiewicz (University of Warsaw) : "What do Sentences State ?"*

Wednesday, June 17—Saturday, June 27

International Plastics Exhibition (at Olympia, London).*

Thursday, June 18

Royal Society (at Burlington House, Piccadilly, London, W.1), at 4.30 p.m.—Mr. F. C. Bawden, F.R.S. : "Viruses : Retrospect and Prospect" (Leeuwenhoek Lecture).

London Mathematical Society (at the Royal Astronomical Society, Burlington House, Piccadilly, London, W.1), at 5 p.m.—Prof. C. A. Rogers : "Coverings of n-Dimensional Space by Spheres".

Antiquarian Horological Society (at the Science Museum, Exhibition Road, South Kensington, London, S.W.7), at 7 p.m.—Mr. D. K. Packard (U.S.A.) : "American Clocks 1780–1840".

Royal Society of Tropical Medicine and Hygiene (at Manson House, 26 Portland Place, London, W.1), at 7.30 p.m.—52nd Annual General Meeting. 8 p.m.—Prof. W. St. C. Symmers : "Clinico-pathological Observations on Some Cases of Fungal Infections and other Tropical Infections met with in Britain" (Series of lantern slides).

Friday, June 19

British Institute of Radiology incorporated with the Röntgen Society (in the Reid-Knox Hall, 32 Welbeck Street, London, W.1), at 11.30 a.m. and 2 p.m.—Radiobiology Meeting.

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned :

Assistant Lecturer in Pure or Applied Mathematics—The Secretary, Queen Elizabeth College (University of London), Campden Hill Road, London, W.8 (June 18).

Assistant Lecturer in Physics—The Registrar, The University, Manchester (June 20).

Assistant Lecturer in the Department of Chemistry and Biochemistry—The Dean, St. Thomas's Hospital Medical School, London, S.E.1 (June 20).

Lecturer or Assistant Lecturer (preferably with a good honours degree in physics, together with research experience in some branch f biophysics or molecular biology) in Biophysics—The Registrar, King's College (University of London), Strand, London, W.C.2 June 20).

Research Fellow in Biochemistry in the Department of Organic Chemistry, for work concerned with enzymic processes related to bacterial cell walls—The Registrar, King's College (University of Durham), Newcastle-upon-Tyne (June 20).

Head (man or woman with medical qualifications and an interest in education) of the Department of Health Education—The Clerk to the Governing Body, Battersea College of Technology, Battersea Park Road, London, S.W.11 (June 24).

Lecturer (Grade II) in Psychology—The Registrar, The University, Bristol (June 24).

Lecturer in Physics—The Secretary and Registrar, University College of North Wales, Bangor, North Wales (June 25).

Lecturer in Sociology—The Registrar, The University, Leicester June 27).

Assistant in Geology, with curatorial duties in the Hunterian Museum—The Secretary of University Court, The University, Glasgow June 30).

Lecturer in the History of Science—The Registrar, The University, Leicester (June 30).

Head of the Plant Genetics Section—The Academic Secretary, Weizmann Institute of Science, Rehovoth, Israel (July 1).

Research Students (with the degree of Bachelor or Master of a British university other than Manchester) in Science—The Registrar, The University, Manchester 13 (July 1).

Lecturer (qualified in chemistry, with teaching experience) in Education—The Registrar, The University, Sheffield (July 4).

Vice-Principal (graduate of a British university (any field), ubstantial teaching experience and some administrative and/or industrial experience)—The Principal, Reading Technical College, King's Road, Reading (July 6).

Reader in Indian Philosophy at the School of Oriental and African Studies—The Academic Registrar, University of London, Senate House, London, W.C.1 (July 8).

Senior Lecturer or Lecturer in Mathematics, and a Senior Lecturer or Lecturer in Chemistry (preferably Inorganic Chemistry) at University College, Ibadan, Nigeria—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (July 10).

Lecturers or Assistant Lecturers in Zoology at the University of Malaya (Singapore Division)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (July 15).

Lecturer/Senior Lecturer in Biochemistry at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 18).

Senior Lecturer/Lecturer (with good general experience in the teaching of zoology and preferably a special interest in vertebrate zoology) in Zoology at the University of New England, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 22).

Lecturer (preferably with a special knowledge of palæontology) in Geology at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 31).

Lecturer (with a higher degree with botany as the major subject) in Botany at the University of Queensland, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 31).

Lecturer in Mathematics at Canberra University College, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, August 1).

Senior Lecturer in Petrology and Mineralogy at Canberra University College, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, August 1).

Senior Lecturer in Physics at Canberra University College, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, August 1).

Chairs (2) in Physics in the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, August 3).

Chair of Zoology in the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (New Zealand, August 31).

Lecturer in Psychology at the University of Melbourne, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, August 31).

Agricultural Officer (Teaching) (with a university degree in agriculture with farming experience and a diploma in education and/or teaching experience) in Uganda to teach general tropical agriculture to students taking a three-year course approximating to N.D.A. standard—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/9/028.

Assistant Lecturer, Grade B (graduate, preferably with teaching or industrial experience) in Physics—The Principal, Medway College of Technology, Horsted, Maidstone Road, Chatham, Kent.

Junior Technical Officer or Technical Officer (preferably aged 24–30, with H.N.C. in electronic engineering or equivalent qualifications, and preferably with experience of the electronic and development departments of the electronic instrument industry), to work on the design and development of electronic apparatus and instruments for use in medical research—Dr. F. D. Stott, Churchill Hospital, Headington, Oxford.

Lecturer, Grade B (graduate of a British university) in Spectroscopy—The Clerk to the Governing Body, Battersea College of Technology, London, S.W.11.

Lecturer (preferably with qualifications in zoology and teaching and/or research experience) in Biology in the Training Department—The Warden, Goldsmiths' College (University of London), New Cross, London, S.E.14.

Lecturer (with an honours degree in physics and preferably some industrial experience) in Physics, to work mainly with National Certificate courses in Applied Physics and Engineering courses—The Principal, Cambridgeshire Technical College and School of Art, Collier Road, Cambridge.

Master to teach Physics—The Headmaster, Trinity School of John Whitgift, North End, Croydon.

Organic Chemist (with a good honours degree in chemistry and postgraduate experience), to take charge of a small team concerned with the development and manufacture of compounds labelled with radioactive isotopes, in particular sulphur-35—The Personnel Officer, The Radiochemical Centre, U.K.A.E.A., Amersham, Bucks.

Senior Laboratory Assistant (preferably with experience in chemistry), to supervise the running of the new, well-equipped science laboratories—The Senior Science Master, Uppingham School, Uppingham, Rutland.

Senior Technician (preferably with experience in biochemical or physiological techniques in man and animals), to take charge of the Medical Unit Laboratories under the Professor of Medicine—The Secretary, St. Mary's Hospital Medical School, Paddington, London, W.2.

REPORTS and other PUBLICATIONS

(*not included in the monthly Books Supplement*)

Great Britain and Ireland

Philosophical Transactions of the Royal Society of London. Series A : Mathematical and Physical Sciences. No. 993, Vol. 251 (12 March, 1959) : Cubic Forms in Thirty-two Variables. By Prof. H. Davenport. Pp. 193–232. 12*s.* 6*d.* No. 994, Vol. 251 (12 March 1959) : Spherical Gravitational Waves. By W. B. Bonnor. Pp. 233–271. 12*s.* 6*d.* No. 995, Vol. 251 (12 March, 1959) : Electrical and Thermal Resistivity of the Transition Elements at Low Temperatures. By G. K. White and S. B. Woods. Pp. 273–302. 9*s*. 6*d*. (London: Royal Society, 1959.) [123

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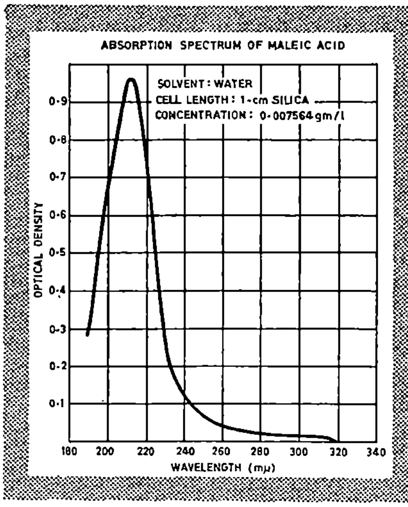

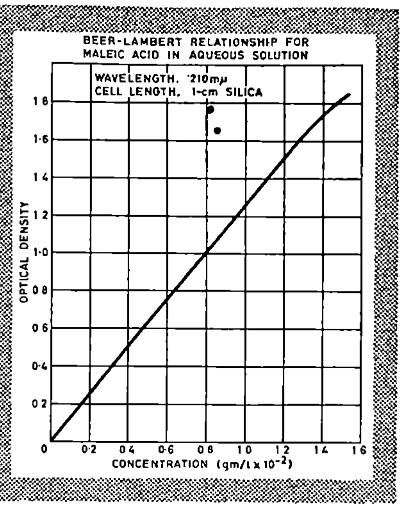

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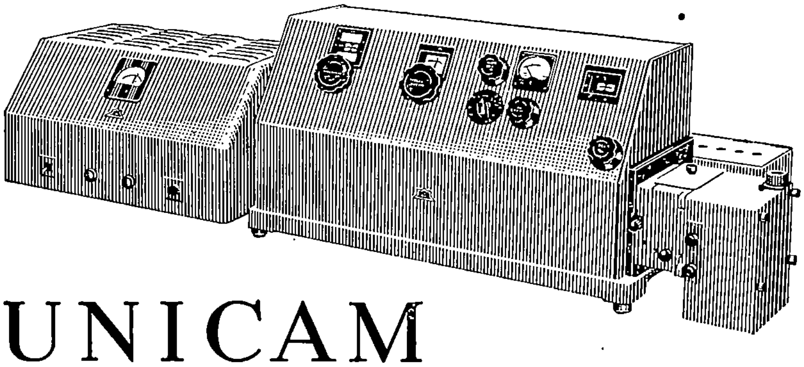

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THE COUNCIL FOR SCIENTIFIC AND INDUSTRIAL RESEARCH

THE annual report of the Council for Scientific and Industrial Research for 1958* follows the pattern of the Council's first annual report last year. Shorn of the detail of the work of the various research boards and stations, it continues the review of the Department's activities commenced in 1957; but, as Lord Hailsham notes in his introduction, it is mainly concerned to indicate the broad features of the plans of the Department for the five years 1959–64. These involve a 70 per cent increase in the expenditure of the Department, from £36 million in 1954–59 to £61 million in 1959–64, rising fairly uniformly from about £9 million in 1958–59 to £14 million in 1963–64, and envisaging a 30 per cent increase in staff (at present 4,860).

The proposed expansion covers all the main fields of the work of the Department, including the activities of its research stations, increased grants for research and postgraduate training in the universities and elsewhere and allowance for increased grants to the industrial research associations, as well as greater efforts to secure the proper communication to industry of the relevant scientific knowledge available. In regard to industrial research, the Council believes that valuable ideas exist in some of the smaller industrial concerns of Britain which they themselves cannot afford to investigate, and that at the other end of the industrial scale there may be research and development projects so big that even large organizations cannot adequately finance them. As to how many of these would be appropriate subjects for Government backing the Council is non-committal; but the Department is ready to consider proposals for the support of industrial research and development, whatever the scale, which are likely to lead to results of value to the nation as a whole.

Although, however, the position of the grant-aided research associations is discussed in about three pages of the report, the work of these associations is to be the subject of a separate report and the general policy towards them is more appropriately and effectively considered when that report appears, particularly since the relevant financial information is to be published in that report. A similar consideration largely applies to the section dealing with scientific and technical information, including overseas liaison, though here we are still without promise of a relevant report. It is stated that during the next five years the Council envisages an expansion of information and advisory services, to ensure that the results of the research carried out in the Department's own stations and in the research associations are more widely known and applied. Funds are being set aside for special assistance of this kind to industry, and it is intended to make every effort to combine the various media of communication, and to link the contributions of the many different bodies concerned, in an effective manner.

One of the grant-aided associations, namely, Aslib, is, of course, specifically concerned with such work, but nevertheless the Council for Scientific and Industrial Research continues to shroud such activities largely in secrecy. No information whatever as to the magnitude of expenditure in this field is disclosed in the present report, other than that in the next few years it will average three times the present figure for the new National Lending Library. While it could not be expected that a report of this general nature should enter on the details which would facilitate effective public discussion, for example, of the plans of the Department for the National Lending Library for Science and Technology, for regional information centres, or for new information techniques, such discussion is particularly important in order to enlist the co-operation and the informed criticism which are essential for the most effective use of man-power and material resources in this field. A reasonably detailed review of activities in this field is overdue and could make an important contribution to eliminating waste of effort and securing the most efficient use of the resources of the Department.

For the rest, apart from the five-year plan, the Council's report continues its review of selected research stations and sets forth the considerations at present guiding its policy in scientific grants. Of the plan itself, Lord Hailsham expresses the view that it should stimulate the growth of science in Britain as a whole and be of great potential value in assisting British industry to keep in the forefront of new ideas, materials and processes and to equip itself technically for effective competition in world markets. In the main, expansion has been planned along the general lines proved by experience, but the Council stresses the importance of not tying expansion too closely in advance to specific projects. While it considers that the present expenditure of the Department is small in relation to the importance of its work, and that, subject to the efficient use of resources, this expenditure should rise as more scientists and technologists become available, it stresses also the need for flexibility. It seeks as much flexibility as possible in allocating its increased funds and in deploying the extra man-power those funds will provide.

The emphasis placed on experimenting with new ideas and amending policy and organization as the need arises is thoroughly sound, though different opinions may well be held as to the accuracy with which research needs can be estimated two or five years ahead and as to the importance—indirect as well as direct—of stability in research policy. The rapid expansion of grants for research and postgraduate training is, of course, aimed directly at increasing the number of scientists and technologists who have pursued advanced studies, as well as at encouraging a healthy and vigorous growth of research in the universities and similar institutions. It is proposed, for example, to double the total number of the studentships awarded by the Department from about 1,900 in 1958–59 to 3,800 in 1963–64, with an even more rapid expansion in grants for special researches, to maintain a healthy balance between teaching and research in the expected growth of academic institutions and to ensure that talent for research is not cramped by the lack of equipment and ancillary staff.

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* Department of Scientific and Industrial Research. Report of the Research Council for the year 1958. Pp. 61. (Cmnd. 739.) (London: H.M. Stationery Office, 1959.) 3*s*. 6*d*. net.

Total expenditure in this field is planned to rise overall to three or four times as much, with considerably greater increases in selected fields. Expenditure in nuclear physics will provide for the maintenance, operation and development of large particle-accelerating machines at six British universities and for one or two new ones, as well as for research designs to secure the maximum benefit from such machines in the universities, at the National Institute for Research in Nuclear Science, and at the European Organization for Nuclear Research. Moreover, the importance of the contribution which the Department of Scientific and Industrial Research is making to our scientific research effort will be enhanced by the Council's proposal to give financial support for longer terms than was customary in the past to outstanding university investigators embarking upon promising lines of research for which the universities cannot make adequate provision. The new policy contemplates grants, where appropriate, for initial terms of three to seven years, terminating with a quinquennium of the University Grants Committee but renewable for one or two quinquennia.

The initiative for setting up these research groups will usually come from the universities, and normally each will be led by an outstanding worker in his field who is on the permanent staff of the university. This new policy, moreover, is the outcome of agreements with the other grant-awarding bodies as to the general principles which should guide the policy of the Council, and the further implications are being considered with the University Grants Committee and the other research councils. It is also hoped to encourage the growth of research teams in the human sciences more comparable with those that already exist in the natural sciences and to attract research workers of high calibre to this field. The Human Sciences Committee of the Council, which in the 1957–58 session recommended new awards and contracts totalling £53,000, is making a thorough survey of research needs, so that it may concentrate resources on a limited number of important topics, each of which falls within the province of one existing research team.

Trends in scientific grants to which the Council directs attention include the maintenance of the high standard of scholarships with the growing number of research studentships and the increasing administration by the Council of awards for the interchange of British postgraduate students in science and technology, with a limited number from funds to be provided through the North Atlantic Treaty Organization. The expenditure on grants of the Research Grants Committee rose from £476,000 in the final year 1957–58 to £617,000 in 1958–59, the increase being greatest in subjects other than nuclear physics. The Council is seeking to strike a better balance of expenditure between nuclear physics and other branches of science and technology, and here again, although the number of recommended awards rose from 115 totalling £856,000 in the previous year to 147 totalling £1,037,000, the quality of the applications was well maintained. Seven specialist subcommittees covering astronomy, biology, chemistry, geology and geophysics, mathematics, physics and technology are advising the Research Grants Committee, and in 1959 the Department is likely to be called upon to administer certain international funds for grants falling within the general province of the Research Grants Committee, such as the scheme of Senior Visiting Fellowships of the Organization for European Economic Co-operation and the Advanced Study Institutes of the North Atlantic Treaty Organization.

The Council's continued survey of present and projected research at the research stations of the Department has confirmed its view that there is a large and growing field for research appropriate to these stations, and that these stations should continue to undertake three types of research of great importance to the nation but of too general an application to be financed by any one industry or group of industries. First, there is research which assists central and local authorities to supply essential services and protect the welfare of the people. Then there is research which improves the efficiency of the economy as a whole; and lastly, comes research which provides industry with basic information for carrying out the applied research necessary to solve its particular problems.

These generalizations, and what has already been indicated as to the Council's policy in regard to scientific grants and the encouragement of research at the universities and similar institutions, including the colleges of technology, show very clearly the firm place the Department now holds in the scientific effort of Great Britain, and the varied but flexible contributions which the Council seeks to make with the modest resources at its disposal. They will not, indeed, dispose of all the difficulties. It may well depend on particular and changing circumstances whether the necessary effort is best made through the Department itself or in some other way. Nothing in this report touches on the unresolved issue of whether research affecting some essential service is best organized departmentally or through a central research department such as the Department of Scientific and Industrial Research. Changing circumstances may also determine whether the Department should enter on some particular field, or whether it is better left to a particular industry or to a university, with or without assistance from the Department.

When the criticism which Sir Hugh Beaver advanced before the Institution of Chemical Engineers a year ago is discounted to the limits of prudence, it is clear that the Council of Scientific and Industrial Research is becoming better equipped to advise on the distribution of Britain's research effort, and probably to advise on some probable effects of such a decision as that recently announced to enter on a programme of space research. The Council obviously is taking flexible views of its responsibilities and is prepared to vary its decisions and policy with changing circumstances.

The Council is anxious to remove any doubt as to the purpose of the National Chemical Laboratory, which is to undertake selected basic and applied research of national importance not being conducted elsewhere and inappropriate to any other organization. The Laboratory does not exist to cover the whole field of basic research in chemistry, and its resources are now to be concentrated fairly rigorously on a limited number of objectives. In future, these will comprise, first, problems requiring research of a fundamental nature which are of importance to the advancement of scientific knowledge and the development of industrial processes but which are inappropriate to universities and other research organizations because of the special facilities, experienced staff and continuity of effort required. As examples are cited the determination of fundamental physico-chemical properties of materials required by chemical engineers in the design of full-scale plant.

A second category comprises problems the solutions of which are of considerable importance to many industries and to the national economy, such as the control of the corrosion of metals, which could offer annual savings of several hundred million pounds. The third category is concerned with chemical researches carried out for other organizations on a repayment basis; of these, the research being undertaken for the Atomic Energy Authority on the extraction of elements of importance for the production of nuclear power from low-grade ores is at present the most important. It is in accordance with this policy that the work of the National Chemical Laboratory in the high-polymer field is being confined to work on polymer membranes and to the synthesis of resins for special purposes such as the separation of metals, and that the chemical engineering work is being transferred to the new Warren Spring Laboratory at Stevenage.

The first two categories of work appear to be pre-eminently the type of research with which the research stations of the Department in general should be concerned, and the new departure in financing chemical engineering research recently announced by the Association of British Chemical Manufacturers and the British Chemical Plant Manufacturers' Association is of some interest in this connexion. This decision is the outcome of the report of a distillation panel set up by the Chemical Engineering Research and Advisory Service Committee of the former body to recommend some basic researches, and at the moment £10,000 a year is being spent by the two Associations on six research projects at four British universities. It represents a new departure in co-operation in research of which the Council of Scientific and Industrial Research must clearly take notice, and one which could well affect the activities both of the Warren Spring Laboratory and of the Mechanical Engineering Research Laboratory (since renamed the National Engineering Laboratory), where it is proposed both to expand the resources of the Laboratory over the next five years and to concentrate on fewer projects.

In such a context the decision to make a deputy director both at the National Physical Laboratory and at the National Engineering Laboratory primarily responsible for fostering close relations with industry may prove to be of particular importance. The Council has also reorganized the Electricity, Metrology and Physics Division of the National Physical Laboratory, together with the Test House, on a functional, instead of a subject, basis in those Divisions: Standards, Applied Physics, and Basic Physics. The last is responsible for pioneering developments in certain branches of modern non-nuclear physics which have potential applications in industry, and the Council believes that the programme of fundamental research in new fields now taking shape will attract a strong team of able young scientists to the Laboratory.

While the Department has now largely shed its responsibilities for research on timber and on food, it accepted on April 1, 1959, responsibility for the Tropical Products Institute. This research station will continue to seek to improve the economic viability of the undeveloped territories of the tropics, primarily those that form part of the Commonwealth, and to advance the technology of existing industries as well as the introduction of new industries by means of research into new uses for tropical plant and animal products. Such work will continue to be supported from Colonial Development and Welfare Funds, and the new arrangement should strengthen the relations already existing between the Department and the Colonial Research Council and the Colonial Products Council; but equally it indicates the need for the Council of Scientific and Industrial Research to be considering closely the location and organization of Colonial research.

This second report of the Council for Scientific and Industrial Research should remove some of the misunderstandings as to its work and responsibilities which have been freely expressed in recent years. It does not, indeed, deal with the question of the direction or distribution of the scientific and research effort of Britain at the highest level; but it does suggest that, within its own field and limits, the Council is well qualified to strengthen that effort not merely in specific or particular ways but also frequently to restore the balance, for example, between research in nuclear and in non-nuclear physics, and to provide flexibility and variation. The sixty pages of the report contain ample material for informed discussion of many aspects of Britain's effort in scientific and technical research.

SCIENCE AND SOCIETY

Our Debt to the Future

Symposium presented on the Seventy-fifth Anniversary, 1957. Edited by E. G. D. Murray. (Royal Society of Canada "Studia Varia" Series, Vol. 2.) Pp. viii+133. (Toronto: University of Toronto Press; London: Oxford University Press, 1958. Published for the Royal Society of Canada.) 32*s.* net.

THE papers which have been collected under the title "Our Debt to the Future" cover a wide field. In these general addresses the Governor-General, Rt. Hon. V. Massey, puts some pointed questions to Fellows of the Royal Society of Canada and suggests that they might concern themselves more closely with the whole intellectual life of the community. The president, Dr. W. A. Macintosh, reviews the development and work of the Society, and Dr. D. L. Thomson discusses the roles of the scientist and the scholar in Canada's future, and there are five other groups of papers. These consider, respectively, the penalties of ignorance of man's biological dependence, the social impact of modern technology, Canada's economic potential in the light of science, human values and the evolution of society, and Canada's human resources.

In spite of this diversity the symposium displays a noteworthy unity and its presentation of the contribution which scientists and scholars can make to national development is markedly free from technicalities, and is a happy demonstration of the possibility of that venture into communication to which the Governor-General summoned the Fellows of the Society. It demonstrates what can be done to ensure that public opinion, and the legislative and diplomatic action it initiates, are adequately informed and to diminish the danger of learning and scholarship being submerged in a technological servitude. It indicates questions to which answers must be sought here as in Canada if our educational institutions are to be shaped to meet the needs of the day, and if a reasonable solution of the problems of power and responsibility, of wisdom and learning, is to be found before disaster falls on us.

Such questions are raised, with the fitting note of urgency, in the Governor-General's address. The presidential review of the past brings into sharper focus the opportunities of the future and the moral and intellectual challenge they offer with its emphasis on cultural and humanistic values as well as adequate scientific and technical knowledge and skill. That is further underlined by Dr. Thomson, who, while deprecating the distinction between the scholar and the scientist, insists that we must both stimulate the spirit of enterprise and adventure in youth, and seek to train men and women not only professionally competent but also having access to those deep wells in which lie the secrets of the future.

The contributions to the symposium dealing with the biological sciences are concerned more specifically with Canadian problems, but they begin and end with a plea that scientists should demand and be granted more influence in the use of their knowledge, more say in determining financial needs for scientific research and some control over the implication of science for political expediency. Mr. R. H. Manske frankly urges scientists to take a more active part in public affairs if only because of the public benefit to be derived from the more objective thinking in public affairs which the whole training of the scientist has been designed to encourage.

Some of the wider issues which are involved in the social impact of technology are discussed in the following symposium. Mr. V. W. Bladen points to problems calling both for research and reflexion, for example, in regard to investment, to leisure, to resistance to change, while Dr. E. W. R. Steacie directs attention to the influence which society itself has on the guiding of technological advance and points out that the development of scientific knowledge and the potential technological advances which may arise from it have given society, for the first time, a chance to make decisions on many matters previously largely or wholly beyond its control. All science can do is to increase the fund of natural knowledge and thus increase our potential control over our environment. What society does with this power is a social problem, and if there is a conflict between the scientist and the humanist to-day Dr. Steacie suggests it is not out of narrowness versus breadth but rather one of understanding Nature compared with understanding man. Mr. W. H. Watson also stresses the need to learn to combine the solid tradition of broad human understanding with an appreciation of the need for new intellectual tools adequate to deal with practical matters. The solution of actual problems is often made more difficult by technical inadequacy of the means available, and many of the men who by endowment, training and experience are entrusted with commenting on the broad human situation are often unable to comprehend the scope of the changes that are imminent. By separating themselves from science they have lost touch with a large and important part of the intellectual life of modern man. Mr. Watson does not claim that the methods of science are the only methods that men may be disposed to use, but he points out that through efficient educational processes new ideas work their way with cumulative effect to cause social change beyond our imagining.

The symposium on science and economic potential, although concerned essentially with Canada's own economic resources, brought to light a divergence between the views of the economist and the specialist in resources or conservation which is of some general interest since, as M. M. Lamontagne remarks, it increases the difficulty of developing adequate policies for the utilization and conservation of resources. That on human values and the evolution of society is of general interest. Dr. T. W. M. Cameron, observing that society, not science, creates technology, that science is part of both culture and humanism, and that the humanist must be able to distinguish between science and technology as well as to control the advances in technology, emphasizes the limited potential of constructive thinkers. We need to remember that man's internal environment is under only partial mental control and that although all potentialities can be developed only a very few individuals can be really educated to be constructive thinkers. Society must seek them out and provide them with the opportunities to develop their particular talents. Far too little attention is still being paid to the human biological sciences, those which concern man as an organism. These views were further elaborated by A. S. P. Woodhouse who, agreeing that education is the principal means of preserving and spreading if not of advancing civilization, urged that such education should in its character reflect and in its operation fortify two of the distinguishing marks of a civilized society: permanence and progress. This debate about the ends of education continued in the concluding symposium, in which J. K. W. Ferguson referred to the danger of demands for universal secondary and even higher education swamping facilities and debasing the product. Diversification of channels for post-primary education should be a practical aim and the maximum freedom of individual choice should be an ideal. Mass media had contributed much at the evocative level of education and they might possibly be used to do even more. L.-P. Dugal suggested that to restore the proper balance between liberal arts and science, thus uniting modern knowledge, was a main responsibility of our time and implied a pattern of education sufficiently flexible, especially in the early formative years, to satisfy later both the needs of the nation and the aspirations of the individuals. Finally, W. B. Lewis took up Dr. Steacie's challenge, how much efficiency did we want, and referred to the importance of finding new ways, especially by the improvement of our means of communication, of helping the universities to deal with increasing numbers without lowering standards. Further, the research institute and the university could and should be mutually helpful. We should ensure that adequate technical aids were available and that more care was taken to see that the tools were appropriate to the purpose so that man-power was used efficiently.

R. BRIGHTMAN

RECENT DEVELOPMENTS IN PLANT PHYSIOLOGY

Annual Review of Plant Physiology

Vol. 9. Edited by A. S. Crafts in association with Leonard Machlis and John G. Torrey. Pp. x+510. (Palo Alto, Calif.: Annual Reviews, Inc., 1958.) 7 dollars.

AS with previous volumes, the Annual Review of Plant Physiology for 1958 covers a wide range of topics. In this volume they extend from the physiology of salt tolerance, reviewed by L. Bernstein and H. E. Hayward, to post-harvest physiology of fruits, discussed by R. Ulrich; from the quantum yield in photosynthesis, dealt with by R. Emerson, to morphogenesis in lower plants, considered by L. F. Jaffe.

In the introduction to this volume, the editor refers to the changing emphasis with time in the field of plant physiology, and among a number of subjects on which emphasis has been laid in the past he includes auxin *a* and auxin *b*. If these have suffered eclipse, the interest in growth substances is as lively as ever, for no less than three of the fifteen reviews which make up this volume are concerned with auxins. J. A. Bentley deals with the naturally occurring auxins and inhibitors, P. M. Ray with the destruction of auxin, and A. C. Leopold with the uses of auxin in the control of flowering and fruiting. The related topic of herbicides is considered by E. K. Woodford, K. Holly and C. C. McCready. The extent of the bibliographies to these four articles, which contain respectively 231, 159, 190 and 357 references respectively, of which only a few are earlier than the year 1950, gives some indication of the current interest in growth-regulating substances.

Two reviews deal with special aspects of plant metabolism. In one of these, L. W. Mapson considers the function of ascorbic acid in plants. The universal presence of this substance in active metabolizing cells suggests that it has some essential function and, although it is not by any means clear what this is, it is useful to have this statement of the present position. Perhaps in no aspect of plant metabolism does fresh information accumulate more rapidly than in nitrogen metabolism, and in this field E. W. Yemm and B. F. Folkes write on the metabolism of amino-acids and proteins in plants, the problems of the synthesis and interconversion of amino-acids and their relation to protein metabolism being dealt with particularly thoroughly.

An article by W. Reuther, T. W. Embleton and W. W. Jones on mineral nutrition of tree crops deals chiefly with the major nutrients, nitrogen, phosphorus, potassium, calcium and magnesium, including the effects of their deficiencies or excess and their relations to quality of fruit. Some data are also given with regard to micro-nutrients and the inter-relationships of the mineral nutrient elements.

The physiology of one particular plant, tobacco, is the subject of a contribution by R. A. Steinberg and T. C. Tso, while the physiology of a whole group of plants, the freshwater algae, is reviewed by R. W. Krause in a paper with a bibliography containing 467 references. The volume concludes with contributions on the biogenesis of flavenoids by L. Bogorad, and on cytochromes in plants by L. Smith and B. Chance.

This volume is well up to the high standard of its predecessors and will be invaluable as a work of reference for plant physiologists wishing to obtain a view of recent developments in those aspects of plant physiology outside their own specialist interests.

W. STILES

MATHEMATICS FOR THE PHYSICAL SCIENCES

Ancillary Mathematics

By Prof. H. S. W. Massey and H. Kestelman. Pp. xvi+990. (London: Sir Isaac Pitman and Sons, Ltd., 1959.) 75*s*. net.

IN the post-war revision of examination syllabuses in the University of London, much attention has been given to the amount and kind of mathematics required to-day by a student whose chief interest is in one of the sciences. While a good knowledge of calculus and differential equations is still necessary, there is an increasing demand for a wider scope and a deeper logical understanding: the scientist can no longer safely rely on a manipulative technique built on sketchy foundations. The present volume is designed to meet present-day needs in physics and chemistry, and should see the student from his *A*-level mathematics as far as the end of his first year at the university. Such a course cannot but be voluminous, since it includes, for example, three-dimensional geometry as far as the elements of differential geometry, spherical trigonometry, differential and integral calculus of functions of more than one variable, the elements of the calculus of variations, as well as a concise but comprehensve treatise on particle and rigid dynamics, using vectors and moving axes, and going as far as Lagrange's equations and variational principles such as Hamilton's. Yet there is nothing superfluous in the book's 1,000 pages; one may even regret that there is no mention of matrices or tensors, and that complex-variable theory stops at the Cauchy–Riemann equations and does not touch on Cauchy's theorem.

Though one may suspect that, of the distinguished authors, the Professor of Physics is responsible for much of the motivation while the Reader in Mathematics has been the keeper of the mathematician's conscience, there is no evidence of any such dichotomy in the book itself. It is an integrated piece of work; mathematical rigour is not something to be taken or left according to taste, it is woven into the stuff and fabric of the volume. Proof is as important to the scientist as it is to the mathematician: "if scientists to-day continue to practise the errors condemned by Berkeley, it is because on most occasions they are content with rules, not proofs" (p. 76). But here and there, when a piece of needed technique depends on a difficult proof, the argument is left in small type, a warning to the reader that there is no royal road.

Every point of importance is illustrated and emphasized by worked examples, and there is a more than adequate supply of exercises for the reader, mainly taken from recent examination papers in the University of London. There can scarcely be a better text-book for the young physical scientist who has realized that Kelvin's demand for "a guid bellyful o' mathematics" is even more urgent to-day.

T. A. A. BROADBENT

ANCIENT IRELAND

Early Christian Ireland

By Máire and Liam de Paor. (Ancient Peoples and Places, Vol. 8.) Pp. 264 (76 plates). (London: Thames and Hudson, Ltd., 1958.) 25*s*. net.

THIS volume of the Ancient Peoples and Places Series lives up to the high standard of production and half-tone illustration we have come to expect from Messrs. Thames and Hudson. The book, presumably intended more as a convenient handbook for the educated layman than as a reference work for the scholar's shelf, is most pleasantly written; so much so, in fact, that one tends to be beguiled by the easy style and to slide, unthinkingly, over some errors of fact and uncertainties of interpretation.

For the layman the volume is adequate and competently handled. With a few exceptions, there is little new in it and there is general adherence to established chronological and art-historical schemes, especially those adapted to an English taste.

A more critical appraisal discloses instances of poetic writing which will be passed over by the foreign reader but which, in Ireland, may cause some questioning. For example, on p. 15, the authors tell us that "all the kings of Ireland . . . could trace their descent from Adam, naming an ancestor in each generation". This is romantic but not strictly accurate: the *fili* may have been able to do this, but not their royal overlords. Again, it is stated (p. 19) that "the highland periphery [of the island] can provide only scattered and separate refuges for older traditions". This is a statement which it is difficult to substantiate. On p. 32 we are told that ". . . it seems likely that the hill-forts of the Iron Age were passing out of use in St. Patrick's time", but we are left guessing as to what these monuments are and what evidence there is for their falling into disuse.

On p. 34 we are told that "the fifth-century missionaries brought the use of letters to Ireland" but on p. 61 the statement is made that the Ogham stones "in a rune-like cipher [it is not rune-like—J. R.] based on the Roman alphabet" are "perhaps as early as the fourth century". In fact, there is some slight evidence, which the authors might have investigated, to suggest that certain classes in Ireland were acquainted with letters at an even earlier stage.

We get general statements such as that on p. 54: ". . . in time the monastic workshops became the chief centres of craftsmanship in the country", a statement for which there is only the slightest archæological evidence, especially when one remembers the special social and legal position of the *aes dána*, the lay guild of craftworkers, and the existence of so many non-monastic *ateliers*, such as those at Lagore, Garranes, Garryduff, etc.

There are several instances of a lack of digestion on the part of the authors of the book, an indication that they have not made up their minds as to what theory they should hold on particular issues. For example, on p. 143, Byzantine and Carolingian iconography is stated to have been drawn upon by the carvers of the scripture crosses and reference is made to the Continental panelled ivories; but no suggestion is made as to the origin of the panels on the high crosses. On the other hand, on p. 154, in discussing the metalwork, it is implied that the panelling is derived from what the authors call the "Trewhiddle style of southern England". This, then, leaves one reader at least facing the question: do the authors mean that the *crosses* are Irish, the scriptural scenes on them Byzantine and Carolingian, and the framework of the panels English? If this is what they mean, it might have been conveyed more clearly, though it might not even then have received general acceptance.

It is a pity that the book contains a fair share of misstatements and errors of fact, most of which could have been checked by reference to the specimens exhibited in the National Museum of Ireland. A few random examples will suffice: (p. 35) the trumpet stated to be from "Annaclone, Co. Down" must be that from Ardbrin, Co. Down; it has no mouth-disk and bears no repoussé ornament; (p. 39) the Boyne bracelet has not an ornithomorphic whorl in red enamel. No enamel remains and there are no birds' heads on the ends of the triskele arms (p. 171). It is the front and not, as here stated, the back of the Cross of Cong which is panelled; and p. 96 contains the extraordinary statement that "crucibles for smelting copper and bronze are fairly common".

It is a pity, too, that elaborate Irish spellings were used when even the reformed Irish spelling would have been phonetically easier. For example, in a work in English, why not use the well-known form of the personal name "Mahon" rather than the ugly-looking (and for most people unpronounceable) "Mathghamhain"; and, if one insists on being traditionally Gaelic in one line, one should strive to be correctly Gaelic in the next by writing "Dál gCais" for the authors' incorrect "Dál Cais".

Finally, why use a term that is as historically meaningless (though current) as "Dark Age", and why apply it to the ninth century in Ireland?

What appear to me as faults in an otherwise excellent production have been pointed out; they are all such as can be corrected in a second edition, for I am sure that a volume that contains as much valuable information as this does, that is as well illustrated and as cheaply produced, will undoubtedly be in demand for a long time. JOSEPH RAFTERY

THE ASTRONOMICAL EPHEMERIS, 1960

By D. H. SADLER, O.B.E.
Superintendent, H.M. Nautical Almanac Office

"THE Nautical Almanac and Astronomical Ephemeris" (usually referred to by its abbreviation, "Nautical Almanac") was first published, by Nevil Maskelyne, the fifth Astronomer Royal, for the year 1767. It has since been published annually under the same title, but with variations of content reflecting the varying requirements of navigation and astronomy. Beginning with the edition for 1960, the title has been changed to "The Astronomical Ephemeris": the volume has been completely unified with the corresponding United States publication, "The American Ephemeris and Nautical Almanac", and further changes of content have been introduced.

A change of title was inevitable: the Almanac has long ceased to serve navigators and, with the introduction of Ephemeris Time, is now still further removed from the requirements of navigation. The title "The Nautical Almanac" will henceforward be used, in the United States as well as in the United Kingdom, for the unified edition of the Almanac for surface navigation previously entitled "The Abridged Nautical Almanac" ("The American Nautical Almanac" in the United States). Thus, the original title is to be regarded not as discontinued but as divided into two parts; the two publications, the astronomical and the navigational, each continue the tradition of the original in both title and content. The present change of title is, in fact, a long overdue consequence of the recognition, so long ago as 1914, that the requirements of the astronomer and navigator could not be met in a single publication.

Unification with "The American Ephemeris" (which still retains its title) follows the similar unification of the navigational almanacs, and sight reduction tables, for both air and surface navigation. It may seem strange that, in this practical form of international co-operation, astronomy should have to follow the lead set by the essentially practical science of navigation, in which national usages and prejudices, especially among the Services, might have created many difficulties. Actually, unification of the astronomical ephemerides has been a very much more elaborate and difficult undertaking than unification of the navigational publications. Without the maximum co-operation and goodwill in both Nautical Almanac Offices it is doubtful if this unification could have been achieved; and the minor imperfections, still to be put right in future editions, bear witness to the countless discussions, concessions and agreements that have been necessary at all stages.

The basis of the unification is that, with the exception of a few introductory pages, the two publications, "The Astronomical Ephemeris" and "The American Ephemeris (and Nautical Almanac)" are identical; they are printed separately in the two countries by photographic methods from reproducible material prepared partly in one country and partly in the other. The sharing of the responsibility, and of the work, in this way is inescapable. However, it does introduce difficulties, which are fortunately of a transient nature, in ensuring complete consistency between the two sections; the few inconsistencies that remain, which the majority of users will not notice, will be removed in future editions. Moreover, this method involves the combination, in the same volume, of two different printing styles and conventions; but the printed volume has proved to be less objectionable in this respect than was at one time feared.

The main object of unification is not the relatively small, but still significant, saving in time and cost of calculation, compilation, printing and proof reading; it is to try to ensure that the basic astronomical data are uniformly available to astronomers everywhere in a consistent form. Advanced proofs of the fundamental ephemerides of the Sun, Moon and planets are distributed to about a hundred organizations throughout the world, and reproducible material for the whole Ephemeris can be supplied on payment of a small charge through H.M. Stationery Office. The German "Berliner (Astronomisches) Jahrbuch", introduced for the year 1775, ceased publication in 1959; astronomers in German-speaking countries will use one or other of the editions of "The Astronomical Ephemeris", with the aid of a German translation of the introductory and explanatory matter.

The main change in the content of the Ephemeris is the adoption of Ephemeris Time, instead of the previous Universal Time (equivalent to Greenwich Mean Time), as the argument for the fundamental ephemerides of the Sun, Moon and planets. Universal Time is measured by means of the diurnal motion of the Sun, and its rate is directly proportional to the rate of revolution of the Earth on its axis; it therefore includes all the irregularities—periodic and secular—of the Earth's rotation. Ephemeris Time, on the other hand, is a measure of the Earth's motion in its orbit around the Sun, and is as nearly uniform as present knowledge permits. The motions of the Moon and planets, which are clearly independent of the irregularities in the rotation of the Earth, can only be predicted theoretically in terms of some uniform system of time measurement, and Ephemeris Time is therefore used. At present, Ephemeris Time at a particular instant is some 35 sec. greater than the corresponding Universal Time; the actual value of the difference between the two can only be obtained by the analysis of observations, mainly of the Moon, and is known only several years in arrear. An extrapolated value is sufficiently accurate to enable most of the other ephemerides to be given with argument in Universal Time.

A full explanation of this and other changes is given in the Ephemeris, and will be further amplified in the forthcoming "Explanatory Supplement" (to "The Astronomical Ephemeris" and to "The American Ephemeris") now being prepared jointly by the two Almanac Offices. Publication, originally arranged for the middle of 1959, has been delayed and will not now take place until about the middle of 1960.

The other changes are not substantial from the users' point of view, but many revisions have been made to increase the precision of the ephemerides—

including the introduction of the 'improved lunar ephemeris' and more consistent ephemerides of the five outer planets, all now given to one additional decimal ($0^{s}\cdot001$ and $0''\cdot01$), and improved data for calculating the apparent places of stars. Users will be most affected by: the considerable extension of the section on "Phenomena", in which are collected, both under individual phenomenon and in the form of a "Diary", the principal astronomical phenomena of general interest during the year; the revised form of the eclipse maps enabling approximate times of the contacts to be more easily read; and the new presentation, by diagrams, of the motions of Jupiter's four principal satellites, which replaces the old method of presentation originally given so long ago as in the edition for 1767. A very few users will miss the ephemerides of the Sun, Moon and planets at transit over the Greenwich meridian; comparison of observation with theory must in future be made with the fundamental ephemerides for 0^{h} E.T. Elements and predictions of occultations are omitted, but arrangements have been made for the publication of the predictions elsewhere; for example, in the British Astronomical Association's "Handbook" and in *Sky and Telescope*. Copies of the elements are supplied to the other national ephemerides.

Frequent changes in astronomical ephemerides are undesirable; apart from details of presentation, and a few minor corrections and 'second thoughts', it is anticipated that "The Astronomical Ephemeris" will remain essentially in its present form for many years.

THE PLACE OF SCIENCE IN UNIVERSITIES PAST AND PRESENT*

By THE RIGHT HON. LORD ADRIAN, O.M., F.R.S.

AFTER his death in 1579, Sir Thomas Gresham's Trustees built an institute in the City of London where he had lived. It was a college for advanced studies, and was opened 360 years ago. It was called Gresham College after its founder, the financial magnate of Elizabeth's reign who built the Royal Exchange. Both arts and sciences were to be taught in it, for it was laid down that there should be seven professors—of music, rhetoric, divinity, law, physic, astronomy and geometry. At that time England had nothing outside Oxford and Cambridge with such liberal aims. Scotland cared more for learning but lacked such great benefactors to support it.

One must not labour the comparison between Gresham College in seventeenth-century London and the Rockefeller Institute in twentieth-century New York. They were both the outcome of individual enterprise and the enlightened disposal of the wealth it had brought. But there is not much more to link them, for the fortunes of Gresham College are too closely linked to the history of seventeenth-century England.

We know very little about the students there but much more about their teachers, for there is a handsome volume on the lives of the Gresham professors published by John Ward in 1748. But we know something at least about the teaching which Gresham wanted the College to give. The regulations for the seven professors ordained that they should inhabit, study and teach there, and that there should be certain several solemn lectures with great care and diligence to be performed by every one of the said lecturers in their several arts and sciences. There was a further regulation drawn up in 1597 which is not without interest still, at all events to the Vice-Chancellors of Oxford and Cambridge. It runs "for that the greater part of the inhabitants within the City understand not the Latin tongue, whereby the said lectures may become solitary in a short time if they shall be read in Latin only; and yet withal it is very likely that diverse strangers of foreign countries who resort thither and understand not the English tongue will greatly desire to hear the reading of the said lectures. It is ordained that each lecture should be given in Latin from 8–9 in the morning and again in English from 2–3 in the afternoon".

So Gresham College started well, but it had both the advantages and disadvantages of being in the City of London, at the heart of affairs during the century when Church and State were in the balance and when the City was the central bastion of the Commonwealth in its fight with the King. There were meetings for the discussion of natural philosophy at Gresham College in 1645; but the business expressly precluded matters of theology and State affairs. Later it was some of those same philosophers who moved to Oxford and met in Boyle's rooms, where "they could converse in quiet with one another without being engaged in the passions and madness of that dismal age".

No doubt it was not so bad for the young men. At all events, after the Lord Protector had established his rule, some of the younger philosophers at Oxford and Cambridge were professors at Gresham College. William Petty was professor of anatomy at Oxford and became professor of music at Gresham College in 1650, and Christopher Wren was made professor of astronomy there in 1657, at the age of twenty-five. But until the Restoration, the City of London must have been an uneasy place for academic studies, and there is no evidence that the lectures were ever regarded as an organized course of instruction for students.

It was after 1660 that Gresham College had the full advantage of its position. The King and many of the Court were interested in the new learning; some of them had occupied their time with experiments when they were in exile, and some of the Oxford philosophers had come to London and were anxious to continue their meetings, and Gresham College was the obvious place for them.

Next year the three-hundredth anniversary of the foundation of the Royal Society of London for Improving Natural Knowledge will be celebrated, and we shall find that its early history is closely bound up with that of the College. Several large rooms were set aside for its meetings and its books and apparatus and curiosities. All kinds of experiments were demonstrated to the Fellows there, and all kinds of new instruments were made by Robert Hooke, the curator. It became the focus for every kind of scientific advance in the Newtonian period.

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* Substance of an address delivered on May 21 at the Rockefeller Institute Convocation for Conferring of Degrees and Dedication of New Buildings (see also *Nature*, 183, 1629; 1959).

The College was something like one of the smaller foundations at Oxford or Cambridge, built around a court or a quadrangle with a cloister on two sides. There were no chapel and no dining-hall, as there were no resident students, but there were a large reading hall and a large west gallery for meetings. There were the lodgings for the seven professors, with an observatory for the professor of astronomy (erected in 1674 at a cost of £40 to "encourage Mr. Hooke in his curious and useful inquiries") and a laboratory for the professor of physic. In Virtue's engraving (dated 1739) there is a curious object standing in the middle of the grass plot and there were the usual stables and outhouses and a row of almshouses in front.

Gresham College might have played an even larger part in the development of science if the advantage of being in the heart of London had not been offset by the disadvantages of being in the City. The Great Plague of 1665 was one, for it made London uninhabitable for a time, but it affected the whole country. It sent Isaac Newton home from Cambridge to the manor of Woolsthorpe to invent the method of fluxions and master the laws of gravitation. But in London the Great Plague was followed by the Great Fire of 1666. Most of the City was destroyed. The College escaped ; but it became a refuge for the homeless, the Lord Mayor and the City Courts and offices, and the merchants and shopkeepers from the Royal Exchange. All that was left for the professors and the Royal Society was the astronomy lodging, and so the Society moved to Arundel House in the Strand. They went back to Gresham College in 1673 when the city had been rebuilt, but twenty years later they left it again, for the College needed extensive repairs and there were plans for rebuilding it. In fact the building remained until 1768, but in 1703 the Royal Society felt it would do better in a house of its own. Gresham College lost the immense advantage of its meetings and of the company of its Fellows, and thereafter its history takes on an eighteenth-century placidity. Its great period had been in the forty years before, when it had fully justified the hope of its founders that it would be "in truth a little University or Academies Epitome, as Rome when it flourished was Orbis Epitome". It had been in truth a great postgraduate centre for scientific advance.

The story of Gresham College is largely the story of its connexion with the Royal Society and with the Fellows of the Society who worked there. It is a story full of personal details about men who were remarkable for much more than their interest in science. It is copiously illustrated by portraits, letters and diaries, and it is about men as talented and as different as Boyle, Pepys, Newton, Hooke, Wren and King Charles II. It seems a pity to leave such distinguished company, but our present concern is with the beginnings of a new college in a new age, three hundred years later.

The Rockefeller Institute is not so large and impersonal that we cannot think of it and its staff in the same intimate terms ; but the great flood of scientific endeavour is now too vast to allow us to think of the individuals who move in it. There are still the giants whose heads stand out above the surface, but for the rest personal details and controversies and habits of life are not our affair. We have to survey the operations of an immense army and to do what we can to see that the troops are properly trained and led in the right direction.

It is, and has always been, the prerogative of the universities to train them. Since the Dark Ages they have been training the most intelligent young people in the way best calculated to make them valuable members of the society they would be in. As Europe became more peaceful and prosperous the medieval rulers needed the priests, and lawyers, and clerks and doctors to carry on the growing business of the State. So there was a great expansion of universities ; but now we have to face another great expansion of universities. Every country demands an increased supply of the men who were needed in the past, with the right training to fit them for the government, administration and trading concerns of the State, and there is the further demand for a new class, for the scientists who are needed to give us the full benefits of our new knowledge of the natural world and of our power to control its forces.

The popular demand is for the engineers and technologists, for they are thought to be the people who will bring immediate prosperity to their respective countries and may succeed in planting the flag of our advanced civilization on planets fortunate enough to be within range. For the medical sciences there is the popular demand for the new discoveries to check some present menace to our health or to prolong our lives beyond five score years.

Perhaps there is no great danger that scientists will be much influenced by demands of this kind. They have been, and will be, trained in universities by academic scientists who are aware of the need to study the foundations as well as to put up the temporary and showy buildings.

I think, however, that there is a danger that comes from the great expansion of scientific effort at the university-level, though it may not be as urgent in the United States as in countries where it is less well supported by private endowment. The danger I have in mind is that the centralized authority of the State will come to play a greater and greater part in directing the nature of university training and that it is likely to canalize the direction of advance in science ; to interfere to some extent with the processes by which we arrive at some entirely new outlook on outstanding problems.

When the philosophers met at Gresham College the world of Nature was all before them and they were just as ready to hear a discourse on the ventilation of mines as one on the elasticity of air. The majority of them were gentlemen of independent means who could please themselves ; and the practical problems, about clocks and navigation and agriculture, gave them new ideas on scientific principles as well as on useful arts. But the advance slowed up in the eighteenth century after its promising start in the seventeenth, and an important factor in slowing it must have been the lack of organized teaching in science and of the students to be trained from the outset for a scientific career.

Our universities collect the ablest students : these teach one another unofficially and they are, or should be, taught more officially by senior members of the university who are themselves engaged in research or have at least a close acquaintance with the research of their colleagues. In an atmosphere of intellectual ferment when investigations may be going on next door in a wide range of science the student has to make his own choice, and it is at this stage in his scientific career (if he is to have one) that the seeds may be sown which will germinate later in new ideas, and in these days there is so much ground to cover that only the most self-reliant student can do without the stimulus of varied and active research departments close at hand and of the contacts with the men who are at work in them.

The difficulty is that active research departments have become far more expensive. If they are beyond the means of a university, whoever has to pay for them may feel that results will come quicker if the research is concentrated in a few well-equipped institutes where it can go on uninterruptedly. The obligation to teach can be a most unwelcome interruption, and there are all kinds of minor distractions which universities impose on their staffs. The result has been that there is now a tendency to weaken the research activities of universities by removing some of the most fruitful fields of investigation to special institutes with little or no duty to teach.

The tendency is not peculiar to science: in Great Britain now there are institutes of historical, legal and economic research as well as those for medical, agricultural and physical sciences, some loosely tied to the university structure and some quite outside it. I must tread carefully on such controversial ground for I know what a valuable part such bodies are playing in this and other countries. I know that the policy of the U.S.S.R. has been to develop scientific research institutes under the Academy of Sciences, and that the size and cost of similar establishments elsewhere would be too great to contemplate on anything but a national basis. Yet I feel sure that we ought to resist too much paring down of our responsibilities for advancing knowledge within the framework of university courses. The most fruitful research team will suffer in the long run if it has no direct contact with the student body, and, quite apart from the claims of scientific research, the student's general education will suffer if it can never come near the growing points of knowledge.

It is, of course, arguable that no line of research lives for ever and that it may be better for a research team to have the immediate advantages of freedom from university duties in spite of the long-range disadvantages. Many of these can be avoided if there is good-will on both sides; but it is easy for ill-will to arise when the two sides work under such different conditions, when the full-time research man at an institute can envy the amenities of a university and a busy university lecturer can find no time to get on with his research. Regrets and envies of this kind are in fact the long-term disadvantage of the separation, for those who have the teaching of students at university-level will lose their enthusiasm if their best products are lured away to research institutes and those who work there may be disheartened if there is no audience to be interested in their discoveries.

It is no doubt inevitable that certain lines of research should be developed away from universities and class-rooms; many in the field of technology and applied science are more the concern of the State and of industry and would only absorb valuable space and administrative effort in a university setting. The important point is that universities should be able to maintain active research departments in the kind of science which deals with general principles and offers no immediate profit to society. It is important because such research will give life to the teaching and even more because special research institutes must work on special problems. An enlightened government or an enlightened director of a research institute may encourage work on fundamental long-range problems, and may sometimes provide a refuge for the occasional genius who cannot teach and wants to be left alone. But universities do not need to be specially enlightened to encourage unprofitable research. We are prepared to applaud our colleagues who spend their talents on the lesser authors of antiquity, and so academic scientists need not excuse themselves if they prefer to neglect the fashionable lines of advance. There is always a need for the kind of scientific research which is dictated by pure curiosity, for a fresh outlook will come more readily when there is no obvious target to fix its direction.

In saying that I confess that I am thinking of a friend of mine who has put new life into an important branch of science by never allowing his official duties in any position to influence the kind of work he should do in it. Most of us lack his detachment; but in a university we should have no scruples about deciding what line of research to follow, whereas away from one the line might be prescribed by authority.

Arguments like these, about the best conditions for promoting new developments in science, are bound to be coloured by personal experience. I have worked all my life in a university and should have been sorry to have moved to an institute with a more specific programme; but I have to admit that many of my colleagues have tried it and that their work and contentment have been none the worse. In the end we have to remember that one of the most compelling reasons for choosing a career in science is not that it will increase our comfort but that it leads into unknown territory. It is an adventure and a challenge to the human intellect, and part of its attraction is that we cannot tell how it will go. It is easy to predict that we shall soon know more about the molecular configuration of the viruses or the temperature of the fixed stars; but there is no knowing what will be found out. We cannot really predict what will be the growing-points twenty years hence, so we cannot predict what will be the best conditions for their growth. We have to plan; but the chief consideration in our planning should be that it is flexible enough to meet unpredictable demands.

The Rockefeller Institute has had many years as a research establishment of just the sort I have been attacking. Its success outside the university framework shows how little one can generalize and how much we should miss if we were tied to a single pattern. It has made great advances in medical science when it was not a university, when it was like Gresham College, with famous scientists to improve natural knowledge but without the full-time students to carry on the torch. Now there are students and courses and degrees, the younger generation to be allowed to see the advance going on and trained to take part in it.

In our crowded universities we might be pardoned for envying such ideal conditions, such handsome buildings, generous benefactors and enterprising direction, but we cannot feel anything but pride at the thought that our family has been enlarged by such a precocious, well-connected infant. The founders of our line, the doctors of Salerno, the lawyers of Bologna and the theologians of Paris if they were here now might compare themselves to the old woman who lived in a shoe and had so many children that she did not know what to do ; but they would all agree that this particular child cannot fail to be a credit to the family. It is a university to lead the way into the unexplored territories of science. The Rockefeller Institute, from now on, will make the best of both worlds, the world of research and of advanced teaching. We can all be glad that it has taken this step, which will ensure that its future will not be less productive than its past.

STRUCTURE OF POLIOMYELITIS VIRUS

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IN this communication we report the first stages of an X-ray diffraction study of crystals of poliomyelitis virus[1-3] ; this work is a continuation of investigations begun by the late Dr. Rosalind Franklin, to whose memory we wish to dedicate this communication. There are two main results. First, we have determined the crystal structure and find that the packing of the virus particles is somewhat different from that suggested by the earlier workers[3]. The second, and more important, conclusion concerns the substructure of the individual virus particle. Here we have been able to determine the number and type of arrangement of protein sub-units in the particle. This result relates to some general principles of virus structure put forward by Crick and Watson[4,5] and to previous work by Caspar[6] and ourselves[7,8] on the structure of some small plant viruses. It suggests that there may be another general principle to be added to those already proposed. Furthermore, the X-ray photographs obtained in the course of the work show, for the first time in a virus investigation, a degree of crystal perfection comparable with that of the lower molecular weight crystalline proteins, and we have therefore also described the improvements in experimental technique which, we believe, made this possible.

The crystallization of the *MEF*-1 strain of Type 2 poliomyelitis virus from ultra-centrifuge pellets was first reported by Schaffer and Schwerdt[1] at Berkeley in 1955, and within a short time small crystals of Types 1 and 3 virus were also obtained by the same technique[2]. These crystallizations are indicative of the high degree of homogeneity achieved in the virus preparations. The methods of purification and the properties of the virus have recently been fully reviewed by Schaffer and Schwerdt[9,10].

Later, the crystallization of Type 1 (Mahoney strain) poliovirus directly from a highly purified suspension during a year's storage at 4° C. was reported[3]. A number of crystals were sufficiently large and well-formed for preliminary crystallographic studies to be made on them by the Berkeley workers. A batch of these crystals, ranging from 0·1 to 0·2 mm. in diameter, were kindly given by Drs. Schaffer and Schwerdt in 1957 to Dr. Franklin for investigation by X-ray crystallographic methods.

Experimental

The crystals were sent to us in phosphate-saline mother liquor (0·11 *M* sodium chloride, 0·01 *M* disodium hydrogen phosphate, *p*H *c.* 7·3) contained in a small specimen tube. They clearly had the same appearance as originally described by Steere and Schaffer[3], but many were rather ill-formed, so that it was not generally possible to identify all the axes of a crystal with any certainty except by X-ray photographs. The larger crystals showed weak birefringence when viewed in a polarizing microscope ; the crystals cannot therefore belong to the cubic system. The crystal morphology and its relation to the unit cell will be discussed elsewhere[11].

The crystals are very fragile and tend to stick to the walls of the specimen tube, but by gentle nudging with the tip of a capillary tube it is possible to prise them loose without much mechanical damage and draw them into the capillary with a drop of mother liquor. The first attempts to mount them in this way in glass capillary tubes were made by Dr. Franklin. They proved unsuccessful, the crystals disappearing rapidly after being introduced into the tubes. Dr. Franklin attributed this to the alkaline reaction of the glass and accordingly tried acid-treated tubes. The crystals seemed a little less unstable but still did not last long enough for an X-ray photograph to be taken.

In view of this experience, when the problem was taken up by us after Dr. Franklin's death last year, it was decided to try some neutral material for mounting the crystals. We have found quartz to be suitable. Thin-walled capillaries of fused quartz are available commercially, and we have found that the crystals will last in these tubes (sealed with wax) without any apparent deterioration for periods of at least two months.

This difference in stability of the crystals when in contact with glass and with quartz does seem to show that glass is alkaline enough to affect the stability of a crystal in the small drop of mother liquor in which it is mounted. We doubt very much that this phenomenon is peculiar to poliomyelitis virus ; the reason why this difficulty does not seem to have been encountered in other investigations of virus crystals is presumably that these were grown, in most cases, from fairly strong salt solutions. On the other hand, the poliovirus crystals were grown in dilute salt solution, and our experience suggests that quartz might be generally useful in mounting other protein or virus crystals which tend to be unstable.

The second improvement in technique which we believe enabled us to obtain good X-ray photographs stemmed from the observation of Steere and Schaffer[3] that the crystals tended to lose their sharpness after an hour or more at room temperature. The crystals have therefore always been kept cold. They were stored and mounted in a cold room at 5° C., and, during the X-ray exposure, a jet of dry air, cooled

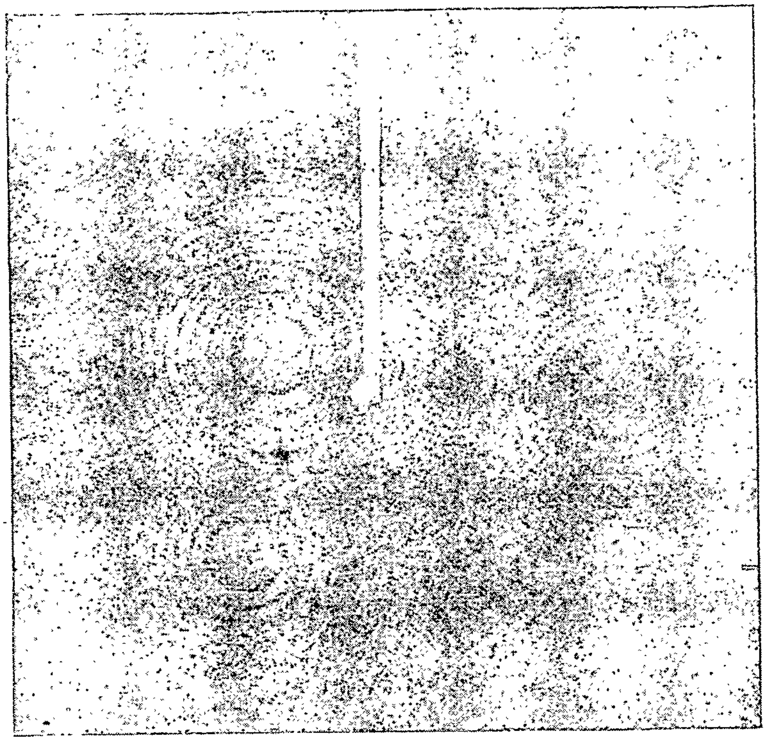

Fig. 1. X-ray diffraction photograph ('still') of a crystal of poliomyelitis virus taken with the X-ray beam approximately parallel to the [110] direction. The perfection of the crystal is shown by the presence of reflexions down to spacings of 2 A.

to about 5° C., was directed on to the crystal in the capillary tube.

There are, however, a number of difficulties attendant on this simple procedure. It is almost impossible to maintain the crystal at exactly the same temperature as its surroundings in the capillary tube. If the crystal is not in the coldest part of the tube, the water in it distils out and the crystal dries and tends to shatter. This will happen even when the crystal lies directly in the direction of the jet but is on the lee side from it. It is therefore essential, if the temperature cannot be maintained strictly uniform throughout the capillary tube for long periods of time, that the crystal be made colder than its surroundings. In this case, however, water from any traces of mother liquor present in other parts of the tube will collect around the crystal and dissolve it. This can be avoided during mounting by expelling the bulk of any excess mother liquor in the tube and mopping up all but a thin film round the crystal with thin strips of filter paper. With these precautions it was possible to keep crystals cold during X-ray exposures of 20 hours or more.

The X-ray photographs were taken with copper radiation from a rotating-anode tube at the Royal Institution, London. Each crystal will only survive a limited number of hours of exposure to X-rays, and can thus, in general, be used for one photograph only. At the beginning of the investigation, therefore, we proceeded by way of 'still' photographs[12], for which the crystal is held stationary. These give the greatest relative amount of information on a single exposure, and enable the axes of the crystallographic unit cell to be picked out on poorly developed crystals with the minimum exposure to radiation. The 'stills' we have obtained from the poliovirus crystals quite generally show crystal reflexions down to spacings of about 2 A. (Fig. 1), indicating a remarkably greater degree of crystal perfection than has been hitherto reported for any other virus crystal. The reasons for this are probably three-fold: first, the original virus preparation was very highly purified[2]; second, the crystals were not only grown in the cold[3] but also never allowed to warm up above 5° C. except possibly for very short times during transfer to the X-ray camera; third, the crystals were not brought into contact with any foreign surface except the inactive quartz. In the early stages of the investigation, a rather high proportion of the photographs showed severe crystal disorder. This we now attribute to mechanical damage, which can be minimized by careful handling.

From measurements on the 'still' photographs, the approximate crystal lattice and cell dimensions were deduced. Thereafter, precession photographs were taken with the X-ray beam parallel to the more important crystallographic directions to determine the crystal symmetry and space group. One of these photographs is reproduced in Fig. 2.

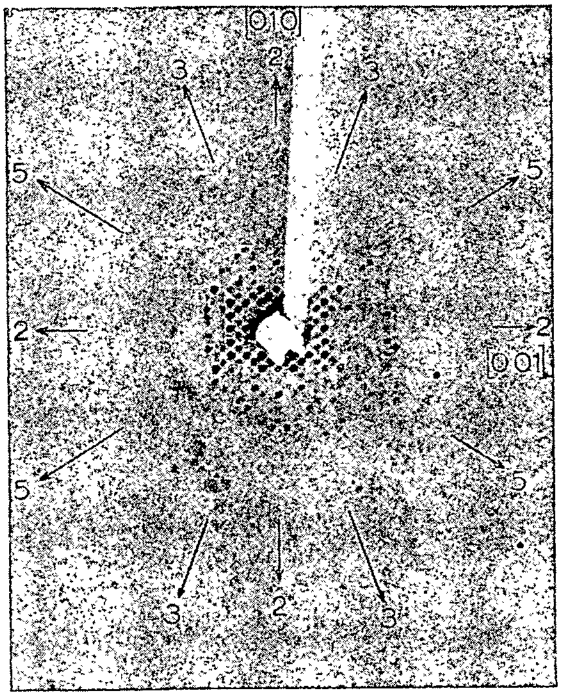

Fig. 2. Precession photograph of a poliomyelitis virus crystal taken with the X-ray beam approximately parallel to the *a* axis. The beam has been set slightly off the axis to show more of reciprocal space within the limits of the precession angle (1½°). The orientations of the 5-, 3- and 2-fold axes of the icosahedral point group 532 which lie in the basal reciprocal lattice plane are indicated by arrows. The intensities of the crystal reflexions tend to be strongest in these directions

Crystal Structure

The axes of the unit cell are at right angles to one another and their lengths (accurate to 1 per cent) are $a = 353$ A., $b = 378$ A., $c = 320$ A. The crystal symmetry is orthorhombic out to the limits of the precession photographs taken so far (0·12 A.$^{-1}$). We cannot rule out the possibility that more data would show small departures from this and that the true crystal symmetry is monoclinic or even triclinic. The discussion that follows must therefore only be regarded as applying to a resolution of 8 A.

At low angles of scattering (down to spacings of about 20 A.) reflexions with $h + k + l = odd$ are absent or very weak, indicating a pseudo body-centring. Since there is not room for more than two virus particles of diameter about 300 A. in the unit cell, the pseudo-space group is $I222$, with two virus particles in the cell, one at the corners and one at or near the centre in the same or nearly the same orientation. There is also the further implication that each particle has three two-fold rotation axes parallel to the crystals axes, that is, it has at least the symmetry of the point-group 222, and hence a minimum of four sub-units.

The general occurrence of hkl reflexions at higher angles, however, means that there is a departure from a true body-centred lattice involving either a slight displacement or rotation of the virus particles. The only possible primitive orthorhombic space-group which permits an approximate body-centred arrangement of this kind is of the type $P2_12_12$. Here the virus particle is required to have at least one two-fold axis which lies along the dyad of the space group. However, we have not been able to determine whether the latter direction is parallel to the a, b or c axis of the unit cell, since none of the $h00$, $0k0$ or $00l$ reflexions observed is of odd index. Furthermore, from the fact that there are also no systematic absences in the $0kl$, $h0l$ or $hk0$ reflexions at high angles, it is possible to show that the departure from true body-centring probably involves a combination of both displacement and rotation. Rough calculations show that a rotation of the particles through a few degrees about the crystal dyad and a displacement of only 10 A. in a direction parallel to the dyad would be enough to produce the observed departures from body-centring. We have not, as yet, been able to specify the crystal structure more closely.

The packing of the virus particles in the crystal is illustrated in Fig. 3. The balls representing the two virus particles in the unit cell have been painted differently to indicate that those of one colour do not lie exactly at the body-centres of the lattice formed by those of the other colour. If the small deviations concerned are ignored, each virus particle is surrounded by 8 others at a centre-to-centre distance of 304 A. This distance is, as one would expect, a little larger than the value of the diameter (273 A.) obtained from electron micrographs of the frozen-dried particle[13] and of replicas of frozen crystalline arrays[3]. In the (110) and (1$\bar{1}$0) planes of the crystal the virus particles pack very nearly in a regular hexagonal array (see Fig. 3), but successive layers are not close-packed together, being displaced over each other so that each particle lies almost symmetrically over a pair in the layer below. Since the sides of the unit cell are not very different from their mean value of 350 A., the crystal lattice may be thought of as pseudo-cubic. Indeed, the departures from a body-centred cubic arrangement are relatively so small as to make one wonder why the crystal symmetry is not strictly cubic, in view of the fact, discussed below, that the virus particle itself possesses cubic point-group symmetry. We hope to return to this problem at a later date.

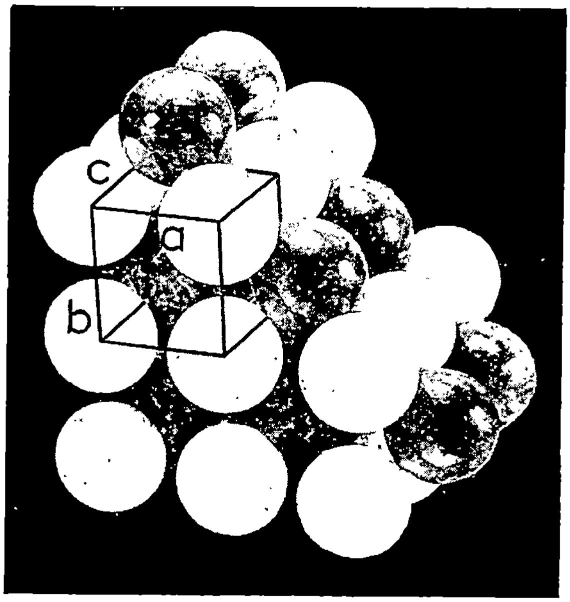

Fig. 3. Model of the crystal structure. The unit cell is orthorhombic with edge-lengths $a = 353$ A., $b = 378$ A., $c = 320$ A. The virus particles are represented by ping-pong balls. The particles fall into two crystallographically distinct sets (see text), indicated in the model by different colours. The sloping face in the model is the (110) plane in which the particles are very nearly close-packed. It is faces of this form that are most strongly developed in the crystals

The structure we have deduced from the X-ray photographs is thus different from the face-centred cubic arrangement proposed by Steere and Schaffer[3]. Their conclusion was, however, based on two sets of measurements on crystals that had undergone some special treatment. First, interfacial angles were measured on crystals that had been previously embedded in clear cement. A distortion of the crystal structure is quite likely in these circumstances. (The crystals sent to us were too small for external crystallographic measurements. It is, however, possible to relate the form development of the wet crystals to the internal structure. This will be discussed elsewhere[11].) Their second set of observations was made with the electron microscope on replicas of crystals that had been previously frozen very rapidly. The beautiful electron micrographs obtained show quite clearly a face-centred-cubic packing of the particles. There is, however, no compelling reason for believing that the structure of the wet crystals is necessarily preserved during the freezing, no matter how rapid. Indeed, one might well expect the contrary to happen, even though the virus particles themselves may not suffer any appreciable damage by the technique. At this point we might remark that electron microscopy has not, in general, given results on the crystal structure of viruses that agree with those deduced from X-ray measurements on the wet crystals. There are at least two other instances, besides that of poliovirus, where the wet crystal structure has been established as body-centred cubic[6,8]; electron micrographs[14,15], however, invariably show close-packed structures. We see no paradox in this. Only a relatively small

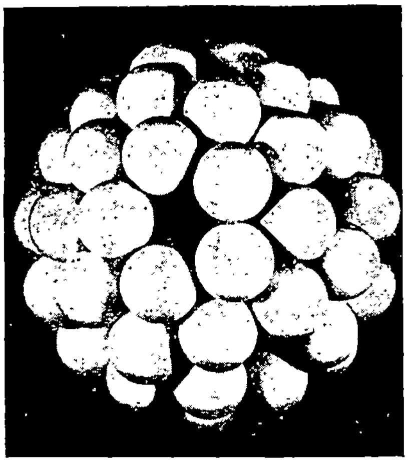

Fig. 4. Schematic model of a likely arrangement of the sixty identical structural sub-units forming the protein 'shell' of the poliovirus particle (cf. ref. 8). The actual appearance of the virus particle will depend on the precise arrangement adopted and on the shape of the sub-unit, which are not known. The diameter of a sub-unit is about 60–65 A.

shear and shrinkage is required to convert a body-centred cubic structure to a close-packed one, and it seems quite reasonable that, under the special treatment of the specimens necessary for electron microscopy (drying, freezing, etc.), the particles should re-arrange themselves to reach the close-packed structure, as the wet structure (held together by relatively weak forces) collapses or is distorted.

Structure of the Virus Particle

Some years ago, Crick and Watson[4] suggested that all small viruses are built up on a framework of protein sub-units packed together in a regular manner. This hypothesis provides a simple explanation of the regular shape of small virus particles, and was based largely on the example of the rod-shaped tobacco mosaic virus. For the 'spherical' viruses, Crick and Watson showed that there were only a limited number of ways in which a round particle could be constructed out of sub-units and that these all involved cubic point-group symmetry. Three types are possible, namely, tetrahedral (23), octahedral (432) and icosahedral (532) symmetry, which respectively imply 12, 24 and 60 identical sub-units. Under the operations of the point-group the sub-units are arranged with their centres on the surface of a sphere, but the appearance of the whole will, in general, be polyhedral.

Shortly afterwards, X-ray crystallographic studies on tomato bushy stunt[6] and turnip yellow mosaic virus[7,8], two small plant viruses containing ribonucleic acid, showed that both particles were cubic in symmetry and, in particular, possessed the characteristics of icosahedral symmetry. In the case of turnip yellow mosaic virus, it was possible, for various reasons, to show that the whole virus particle did not have this symmetry, and it was suggested that the icosahedral symmetry applied only to the protein component of the virus. As a result of more recent work[16] on crystals of the nucleic acid-free top component[17], we have been able to confirm this and to show that the ribonucleic acid of the virus has a lesser symmetry (probably tetrahedral) involving a smaller number of sub-units. (This reference to sub-units in the ribonucleic acid must be interpreted only in a configurational or geometrical sense, not chemical.)

In the case of these two plant viruses it was implied directly by the crystal symmetry that the particle (point-group) symmetry must be at least tetrahedral and so have a multiple of twelve sub-units. No such deduction is possible for poliomyelitis virus; the crystal is orthorhombic and, as we have seen above, this implies only that the virus particle has at least two (or perhaps four) sub-units.

However, the distributions of intensity on the precession photographs of the poliovirus crystals show immediate evidence of a higher particle symmetry. As in the case of the two plant viruses just mentioned, there is a concentration of reflexions of high intensity ('spikes') in directions bearing the same relation to each other as the symmetry axes of the icosahedral point-group 532 (Fig. 2). These must correspond to the transform of the individual virus particle. Because the symmetry of the crystal lattice (222) is lower than that of the individual virus particles (532), the actual symmetry of the transform of a single particle tends to be obscured because it is sampled on reciprocal lattice points which do not have the same symmetry relations as the transform. The examination of five crystallographically independent precession photographs leaves one in no doubt, however, about the underlying symmetry of the transforms. The overall distribution of intensity in the zero-layers of the reciprocal lattice perpendicular to each of the crystal axes should be the same, and this is exactly what is observed in the corresponding precession photographs.

The precession photographs also show that the orientation of the particles in the crystal lattice is such that they have two-fold axes lying parallel to the crystallographic *a*, *b* and *c* axes. The two virus particles in the unit cell both have the same or very nearly the same orientation since there is only one set of spikes. In this respect the structure resembles that of the crystal of bushy stunt virus[6], rather than that of turnip yellow mosaic virus in which particles are present in two orientations at 90° to each other[8]. The crystallographic arguments given earlier require, however, that the two particles be in slightly different orientations, and as a consequence one might expect some 'blurring' or weakening of the spikes. There does not appear to be any such tendency out to the present limits of observation, namely, spacings of 8 A., but to this resolution a feature as broadly defined as a 'spike' of intensity is not likely to be sensitive to slight differences of orientation.

The possession by the virus particles of icosahedral symmetry means that it is built up out of 60 structurally equivalent asymmetric units, but the symmetry alone does not tell us what the actual arrangement of these sub-units is. Some information on this point can be obtained by measurements of the average period of a slow modulation of intensity that is clearly discernible in the precession photographs along the 'spike' directions. This corresponds roughly to the centre-to-centre distance between sub-units in the particle. We find this distance to be 60–65 A., and if the sub-units are roughly globular, this value should give their approximate diameter. If 60 protein sub-units of this size are packed together in fairly close contact, in a way consistent with icosahedral symmetry, they will form a roughly spherical shell of diameter about 300 A., close to that of the poliovirus particle. Hence, on the general grounds set forward by Crick and Watson[4] and by analogy with the established case of turnip yellow mosaic virus, we believe that the protein component of poliovirus is the seat of the icosahedral symmetry.

We still do not know the precise way in which the sub-units are arranged to form the spherical shell of the virus. The ratio of the particle size to the distance between sub-units indicates that the sub-units in the shell are packed very compactly so that each has at least four, and probably five, neighbours in contact with it. The arrangement is therefore probably very similar to that which we have suggested for turnip yellow mosaic virus[8], and which is reproduced in Fig. 4. The actual appearance of the particle will, however, also depend on the shape of the sub-unit, which is not known at present. In electron micrographs, which are of high quality but in which the resolution is still not enough to show individual sub-units, the virus particle will tend to look polyhedral, as is observed[13].

Discussion

The above evidence indicates that the poliomyelitis virus is built up out of sixty identical or structurally very similar protein sub-units. We have added the qualification that the sub-units may not be quite identical since small differences of, say, one or two amino-acids between the protein molecules in a virus cannot be detected by the X-ray method. The molecular weight of the virus has been reported as 6·7 million[9], but in the absence of diffusion measurements this figure must be regarded as only approximate. Of this, about 25–30 per cent is ribonucleic acid[9,10], so that the molecular weight of the protein part of the asymmetric unit is about 80,000. The point-group symmetry does not preclude the possibility of each structural (crystallographic) unit being further subdivided into a number of smaller chemical sub-units ; but there is as yet no chemical evidence at all on protein sub-structure in poliovirus. Our results indicate that a search for such evidence, on the lines already applied to the plant viruses[18], would be desirable.

Our results may further help to clarify the understanding of the various components observed[2] in density-gradient ultra-centrifugation of fluid from tissue cultures infected with poliomyelitis virus. It seems very likely, by analogy with the top component[17] of turnip yellow mosaic virus, that the slower sedimenting, non-infectious, nucleic-acid free fraction designated[2,10] *C* consists simply of empty protein 'shells'. This would explain why electron micrographs of fraction *C* show particles of about the same size but flatter and less sharply delineated[19] than the intact virus particles of fraction *D*. The still lighter fraction *B*, which is immunologically related to *C*, very likely consists of groups of sub-units. Likewise, it is very probable that the 'soluble antigens'[20] that have been observed in extracts from infected cells are related to the protein sub-units used in building the complete infective virus. As for the 'small infectious component' the existence of which has been claimed by some workers[21], it is difficult to see how such particles could be consistent with the model of virus structure described in this paper. There is no suggestion at all from the present work that poliomyelitis virus is made up of more than one nucleoprotein unit.

From the present X-ray evidence we can conclude nothing directly about the structure of the ribonucleic acid of the virus. There is very little on our photographs that is characteristic of its presence in relatively large quantity in the virus. Again, this is quite analogous to the case of turnip yellow mosaic virus, which also contains a relatively high proportion of nucleic acid and the resemblance of which to poliovirus in its structural organization has already been made clear. By the same analogy, we would expect the ribonucleic acid to be located within the shell formed by the protein, and this is in accord with some electron micrographs[22] showing a dense core in the virus. Further X-ray work on the structure of the virus would be greatly facilitated by the separation (or preparation) and subsequent crystallization of protein shells free of nucleic acid (fraction *C*). We would expect the wider considerations of the problem of the structure of ribonucleic acid in ribonucleoproteins, which we have discussed elsewhere[23], to apply to poliomyelitis virus as well.

General Remarks on Virus Structure

Enough has now been said to show that the structure of poliomyelitis virus is of the same kind as that of the small, 'spherical' plant viruses, and bears out the expectation of Crick and Watson[4] that this would be the case. It is probably safe to conclude that there are no structural grounds for distinguishing the smaller animal viruses from the plant viruses.

What could not, however, have been readily foreseen is that the three small viruses the structure types of which have so far been established should all turn out to use only one type of cubic symmetry, the icosahedral, in building their protein shells. This raises the question whether there is not another general principle at work here, and one to be added to those also already put forward by Crick and Watson. We hope to discuss this in more detail elsewhere[16], but the argument may be summarized as follows. The reasons why one might expect small viruses to be made up of sub-units have been clearly stated in Crick and Watson's second paper[5]. The infectivity of a virus is carried by its ribonucleic acid, and the function of the protein part is presumably to provide some form of packaging for the former. The ribonucleic acid controls the formation of the virus protein, and, on current views[24] of protein synthesis, there is a 'coding' of the sequence of amino-acids by that of the nucleotides. There will thus be a limit to the lengths of polypeptide chain produced, set by the ribonucleic acid content of the virus, and the virus protein will be constructed from a relatively large number of small protein molecules. This is where a connexion can be made with the observed icosahedral symmetry, since, of all the types of cubic symmetry, it allows the use of the greatest possible number, namely, 60, of identical structural units in building the framework. Each structural unit may contain in turn a number of chemical sub-units, although these smaller units would not be structurally equivalent since their environments would not all be identical. One might therefore expect the number of sub-units in a small spherical virus to be 60 or a multiple of 60.

The above argument for the occurrence of icosahedral symmetry in virus structures is essentially from a principle of economy. Another, but perhaps subsidiary, reason why the icosahedral might be preferred above the other two types of cubic symmetry is that it probably also gives the most efficient packing of sub-units in a virus particle. If it is required to 'enclose' a space around a point by a symmetrical arrangement of small identical units, it can be shown that the ratio of the number of sub-units to the volume enclosed is smallest if icosahedral symmetry is employed. This is very probably the principle involved in the construction of Tipula iridescent virus, which has been shown by Williams and Smith[25] to have the shape of a regular icosahedron of diameter about 1,300 A. The particle is so large that it is rather like a little crystal, in having plane faces, for example. However, the fact that these faces are related by five-fold axes, which cannot exist in a true space-filling crystal, shows that some features of a point-group structure must be involved.

A number of people have helped to make this work possible. In particular we would like to express our thanks to the following: Drs. Schaffer and Schwerdt for providing us with the virus crystals; Prof. E. T. C. Spooner and Dr. F. Fulton for providing facilities at the London School of Hygiene and Tropical Medicine for storing and handling the crystals; Sir Lawrence Bragg for his interest and for putting at our disposal a rotating-anode tube in the Davy Faraday Laboratory of the Royal Institution, and the members of that laboratory for their generous assistance. This work was supported by a research grant No. *E*-1772 from the National Institute of Allergy and Infectious Diseases, U.S. Public Health Service. We also wish to acknowledge financial assistance by the Agricultural Research Council to one of us (J. T. F.), and a grant by the Wellcome Foundation for the purchase of a precession camera.

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OBITUARIES

Mr. A. G. M. Michell, F.R.S.

Rarely in the history of engineering can theory and practice have been so happily blended as in the person of Anthony George Maldon Michell, the inventor of the thrust bearing, who died in Melbourne, Australia, on February 17.

Michell was born in London on June 21, 1870, while his parents were on a visit from Australia, to which country they had emigrated seventeen years earlier. His early schooling was in Victoria, but at the age of fourteen he accompanied his brother, J. H. Michell (later professor of mathematics in the University of Melbourne, one of the most distinguished applied mathematicians of his day), to Cambridge, and attended some University lectures there after leaving school. Returning to Melbourne, he graduated in civil engineering at the University in 1895.

Michell's early experience, which was in hydraulic engineering, led in 1901 to the invention of the Smith–Michell regenerative centrifugal pump, in which much of the energy of the fluid as it leaves the rotor is used to help drive the pump, thereby increasing its efficiency. Two years later he opened his own office, specializing as a consultant, particularly on hydro-electric schemes; the installation at the Mount Lyell copper mines in Tasmania was the first scheme of this kind in Australia.

At this time the most serious difficulty in the design of water turbines lay in the bearings. No satisfactory way of designing bearings to take an axial thrust along the shaft had been discovered, and they gave continual trouble. Michell made a special study of the theory of film lubrication which Osborne Reynolds had published in 1886, and hit on the novel yet simple idea of using pivoted bearing pads which would automatically tilt and provide the tapered film of lubricant essential in Reynolds's theory. At the same time (1905) in a remarkable paper he extended the theory to the case of the tilting pad. Few major inventions have provided so complete a solution of an apparently insoluble engineering problem: certainly in none can advanced mathematics and engineering practice have been more closely linked.

The thrust bearing was of revolutionary importance not only for water turbines but also for marine propulsion. Shafts could now be designed to transmit twenty or thirty times the horse-power previously attainable, and much larger ships than hitherto became possible. But although it was soon being widely used in Australian installations, the British Admiralty could not be persuaded to adopt it until about 1913 one was accepted by the German firm of Krupp. Thereafter its use rapidly spread in Britain and elsewhere.

In 1911 Michell successfully applied the tilting-pad principle to the construction of journal bearings, and a further most important and ingenious application appeared some years later in his crankless engine, in which reciprocating motion is converted to rotary motion, and *vice versa*, by means of tilting pads against a swash plate. Like the original thrust bearing, these inventions are notable for their simplicity. The crankless engine has never been widely adopted, although it was successful in Australia in various applications.

Among Michell's other inventions were an impulse turbine, a viscometer, the Michell–Seggel floating pad bearing (jointly with his associate, A. J. Seggel) and hydraulic transmission gear. In 1904 he published in the *Philosophical Magazine* a most original paper on the optimum design of framed structures, the importance of which is only now being recognized by aircraft engineers. He was also the author of "Lubrication" and part-author of "The Mechanics of Fluids"—both standard works. He wrote as he thought, with precision, clarity and deep mathematical insight. In 1934 he was elected a Fellow of the Royal Society in the year in which he was first proposed, and in 1943 the Institution of Mechanical Engineers bestowed on him its highest honour, the award of the James Watt International Medal.

Michell never married. Always a modest, retiring man, living quietly with his brother, he was rarely before the public eye. Those who knew him intimately speak of his keen sense of humour, his love of French literature and his wide knowledge of the Australian flora and fauna, which he cultivated at his country home in Victoria. With his passing Australia has lost its most distinguished engineer.

A. J. FRANCIS

Mr. William Hanson, M.B.E.

IN the recent death, at a comparatively early age, of Mr. William Ralph Hanson, head of the London Forecasting Office, the Meteorological Office has sustained the loss of one of its most devoted servants.

Born in 1904 into a family of teachers, he too spent some years in that profession, having graduated B.Sc. in geography while at Birkbeck College; but in 1937 he entered the Scientific Civil Service as a forecaster, serving at various stations in the south of England. He received his commission in the R.A.F.V.R. shortly before the Second World War but did not go into uniform until 1941. Associated intimately with the organization of meteorological services in the North African and Italian campaigns, he quickly reached the rank of squadron leader. It was during this period that he first showed his unusual skill in negotiation and, in satisfying not only the Royal Air Force, the Navy and the Army, but also the Americans in these theatres of war, he performed outstanding services and was mentioned in dispatches.

After the War he accepted an interesting appointment in New Zealand, and while there had his early experience of the routine broadcasting of 'weather', experience which was later to be of such value at home. In 1951 he was posted to Habbaniya, returning to Britain in 1953 to take over control of the London Forecasting Office, where until his death on May 3 he filled a post requiring not only a detailed knowledge of the working of the Meteorological Office and of other Government departments, but also an appreciation of the needs of those, outside the Service, needing weather information and advice, be they in industry, commerce, law, the Press or radio. Under his immediate direction, the automatic telephone weather service for London was inaugurated, the 'weather men' of the B.B.C. Television were put on the screen and the Meteorological Office Centenary Exhibition prepared and sent around the country. Hanson was perhaps at his happiest when dealing with such publicity and was particularly successful in bridging the gap between the anonymity of the Civil Service and the extrovert activities of Fleet Street and Lime Grove, in which places he was regarded with respect and affection. Although he worked mainly in the background, from time to time he broadcast to farmers on television and on the sound programme "The Countryside".

Early promise at the piano, violin and organ indicated a possible career in the musical profession, but of latter years his main interest, apart from Freemasonry, was undoubtedly the London Forecasting Office and the developing of new ways of presenting weather to the public. He engaged in no research and published no papers, but nevertheless was always experimenting in novel forms of presentation, and he will long be remembered for his contributions in this field.

He was much devoted to his wife and four children who survive him.

N. B. MARSHALL

NEWS and VIEWS

The Queen's Birthday Honours List

THE following names of scientists and others associated with scientific work appear in the Queen's birthday honours list:

Baronet: Prof. R. Platt, professor of medicine, University of Manchester, and president, Royal College of Physicians.

K.B.E.: Sir David Brunt, emeritus professor of meteorology, University of London, for services in the organization of the International Geophysical Year; Prof. C. A. Cotton, emeritus professor of geology, Victoria University College, Wellington, New Zealand.

Knights Bachelor: Prof. D. Baird, regius professor of midwifery and gynæcology, University of Aberdeen; L. C. Gamage, chairman and managing director, General Electric Co., Ltd.; Prof. W. V. D. Hodge, Lowndean professor of astronomy and geometry, University of Cambridge; Prof. A. J. Lewis, professor of psychiatry, University of London.

C.M.G.: T. S. Leach, chief inspector of fisheries, Ministry of Agriculture, Fisheries and Food; Prof. J. P. Baxter, vice-chancellor, University of New South Wales, and chairman, Australian Atomic Energy Commission; A. J. Haddow, director, East African Virus Research Institute; J. G. M. King, director of agriculture, Uganda; T. A. M. Nash, director, West African Institute for Trypanosomiasis Research; R. J. M. Swynnerton, director of agriculture, Kenya.

C.B.E.: Prof. W. J. G. Beynon, professor of physics, University College, Aberystwyth, for services in the organization of the International Geophysical Year; W. E. China, keeper of entomology, British Museum (Natural History); Prof. S. J. Davies, dean, Royal Military College of Science; Prof. W. R. Hawthorne, professor of applied thermodynamics, University of Cambridge; Mrs. E. L. G. Hilton, director, Radiotherapeutic Dept., University College Hospital; A. C. Monkhouse, formerly deputy director, Warren Spring Laboratory, Department of Scientific and Industrial Research; E. W. S. Press, director, chemical inspectorate, Ministry of Supply; J. A. B. Smith, director, Hannah Dairy Research Institute; Prof. H. M. Steven, professor of forestry, University of Aberdeen; Major H. Sumner, formerly president, Royal College of Veterinary Surgeons; Prof. L. J. Witts, Nuffield professor of clinical medicine, University of Oxford; Miss Mary Woodall, director, Birmingham City Museum Art Gallery; Prof. N. S. Alexander, professor of physics, University College, Ibadan; C. E. Duff, chief conservator of forests, Northern Rhodesia; C. W. S. Hartley, director, West African Institute for Oil Palm Research; J. D. Pollett, director, Geological Survey, Sierra Leone.

Institution of Mining Engineers: President for 1960–61

MR. R. G. BAKER has been elected president of the Institution of Mining Engineers for the year 1960–61, and will succeed Mr. T. A. Rogers at the sixty-sixth annual general meeting of the Institution to be held in London on January 28, 1960. Mr. Baker, who is deputy chairman of the North-Eastern Division of the National Coal Board, is the second son of the late George Baker, who was a well-known steel maker in the Rotherham neighbourhood. He was educated at the Leys School, Cambridge, and obtained a degree of bachelor of engineering (mining) at the University of Sheffield. After a period as assistant manager at Brodsworth Main Colliery, he became manager at Rotherham Main Colliery in 1934. In 1936 he moved to Earl Fitzwilliam's Colliery Co., initially as assistant manager, and was later successively manager at Elsecar Main Colliery, assistant general manager, and finally general manager of the Company. On nationalization of the coal industry, Mr. Baker was appointed deputy area general manager of No. 3 (Rotherham) Area of the North-Eastern Division and later became general manager of that Area. He was next appointed acting divisional production director of the North-Eastern Division and in 1951 he became deputy chairman of the Division. He has been secretary–investigator of the Coal Dust Committee of the Yorkshire Advisory Committee on Mining Research, a member of the Informal Committee on Shotfiring which was sponsored by the Minister of Fuel and Power, and a member of the Shotfiring and its Alternatives Committee of the Institution of Mining Engineers. Mr. Baker was elected to the Council of the Midland Institute in 1942 and was president of that Institute in 1951–52. He is chairman of the Mining Advisory Committee of the Yorkshire Council for Further Education, and a member of the Mining Qualifications Board.

Cytology at Dublin: Prof. J. Brontë Gatenby

PROF. J. BRONTË GATENBY has been appointed to a new research chair in cytology in Trinity College, Dublin. Born in New Zealand, Gatenby became a lecturer at Oxford in 1916 and in 1917 a senior demy of Magdalen College. In 1920 he was appointed lecturer in cytology in the University of London, and in 1921 to the chair of zoology and comparative anatomy in Trinity College, Dublin. Early in his career Gatenby's immense energy was directed towards the solution of the many problems associated with the study of cytoplasmic bodies and organelles of various organisms. At that time there was little knowledge of extra-nuclear components and inclusions, and Gatenby not only carried out pioneer work but inspired successive generations of students to take up cytological research. Throughout the years he continued to contribute to the understanding of the structure of animal cells, and as new techniques became available in related fields he was always one of the first to adapt these to his own subject. Much of the early work has stood the test of time and forms the background necessary for the advances in cytology that have taken place in the post-war period. Gatenby has not neglected these advances, having, for example, in 1958 visited the Argonne National Laboratory, Illinois. After many years of teaching and research, he relinquishes the chair of zoology and comparative anatomy, and is honoured by appointment to a new research post.

Zoology and Comparative Anatomy at Dublin: Prof. J. N. R. Grainger

DR. J. N. R. GRAINGER, who has been appointed to succeed Prof. Brontë Gatenby in the chair of zoology and comparative anatomy in the University of Dublin, Trinity College, entered Trinity College with a Senior Exhibition and graduated in 1947 with first-class honours in natural science. He was appointed the following year as an assistant lecturer in the Department of Zoology in the University College of Hull, as it then was. While he has been at Hull, he has established and developed the teaching of parasitology in its systematic and anatomical, as well as in its physiological, aspects with great success. Parallel with this work, and in harmony with it, his interests turned progressively towards the consideration in fundamental terms of the mechanisms underlying the capacities of organisms to respond in particular ways to changes in their environment, and in particular to changes in temperature. Of recent years, he has become widely known for his original contributions in mathematical, physical, and chemical terms to the theory of the steady state and its applications to the facts of short-term adaptations in living organisms, and also for the large volume of experimental work which he has achieved in this field. His return to his own University to succeed his old teacher will ensure that the long-established reputation of the Department of Zoology and Comparative Anatomy there for fundamental and original work in physiology will be maintained and extended into new and exciting fields, and that the work of the Department will continue to be securely based on the proper traditions of morphology and systematics.

Bacteriology at Adelaide: Prof. D. Rowley

DR. DERRICK ROWLEY, head of the Department of Bacterial Physiology in the Wright–Fleming Institute of Microbiology, London, has been appointed professor of bacteriology in the University of Adelaide as from December 1, 1959. Dr. Rowley began his professional career during the Second World War as a research chemist, dealing with isolation of intermediate compounds from the 'cracking' of petroleum, and later with improvement in methods for extraction of penicillin. He joined the staff of the Wright–Fleming Institute in 1945, being promoted to his present position in 1953. In 1950, soon after qualifying in medicine, he received a Commonwealth Fund Fellowship for study in the United States. Part of that time was devoted to immunochemical work in the laboratories of M. Heidelberger at Columbia University; the remainder was at the California Institute of Technology, where he studied problems of bacterial genetics with G. W. Beadle. During 1957–58 he returned to America as visiting professor of microbiology at Stanford University. Dr. Rowley's investigations in the field of microbiology began with work on the mode of action of penicillin, with special attention to the binding of penicillin to bacterial cell walls. Later he became interested in the non-specific effects on resistance to infection caused by injections into animals of bacterial lipopolysaccharides. This has led over the past few years to an intensive study on the general problem of natural resistance to infection with particular reference to the roles of such factors as complement, properdin, phagocytosis and so-called natural antibodies.

University Research in the United States

"SCIENTIFIC Research and Development in Colleges and Universities: Expenditure and Manpower—1953–54" (pp. iii+173. Washington, D.C.: Government Printing Office, 1959. 1 dollar) is the final part of the National Science Foundation's survey of the overall research and development effort of the United States in that period. The expenditure of American colleges and universities proper is estimated at 277·7 million dollars (of which 142 million dollars were from the Federal Government), with another 74·2 million dollars at the agricultural experimental stations and 130 million dollars at Federal research centres. Of the first figure, 205·5 million dollars are budgeted separately for research and development, 20·9 million dollars represented indirect costs of such work borne by colleges and universities and 51·3 million dollars departmental research. Of the total 481·9 million dollars, 229 million dollars were devoted to basic research. Colleges and universities, including agricultural experimental stations, employed 62,251 in science faculties, and of these 31,455 were engaged in research and development, while Federal research centres employed 5,000 research personnel. Of the science faculties, 8,300 were engaged full-time in research and development and 42,700 full-time staff were engaged in teaching, research and community service, while 11,300 part-time staff were engaged primarily in teaching. The physical sciences claimed 41 per cent of the total financial provision and 33 per cent of man-power, the biological sciences (including agriculture) 48 per cent of the expenditure and 52 per cent of man-power. Of the total science faculties, 37 per cent were employed in the physical and 40 per cent in the biological sciences. In the 190 large colleges and universities, known to conduct sponsored research projects and granting most of the advanced degrees in science, the physical sciences accounted for 60 per cent of the expenditure and 40 per cent of the man-power, the corresponding figures for the biological sciences being 33 per cent and 47 per cent.

Association of Universities of the British Commonwealth

THE report of the Executive Council of the Association of Universities of the British Commonwealth for the year ended July 31, 1958 (pp. 25. London: Association of Universities of the British Commonwealth, 1959), records that in 1957–58 the Association was asked to act in connexion with 651 appointments in member universities outside the United Kingdom, compared with 408 in 1956–57, and that the office handled 4,149 inquiries regarding advertised appointments. Advisory committees were set up for 51 appointments and reports on 94 candidates were forwarded to the universities concerned. The report refers to the work of the Association, its Council, or Secretary in connexion with Commonwealth University Interchange, Marshall Scholarships, the Frank Knox Memorial Fellowship, British Memorial Fellowships established by public subscription in Victoria, Australia, and Imperial Relations Trust Fellowships, and subjects discussed at the eleven meetings during the year of the Committee of Vice-Chancellors and Principals of the Universities of the United Kingdom are indicated in an appendix.

The Ciba Foundation

THE report for 1958 of the Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research (pp. 25. London, 1959) records that during the year 835 visitors from thirty-six countries were provided with accommodation for short periods. Twelve evening discussion meetings were held, covering bioenergetics; mammogenic and lactogenic activities of the placenta; selective toxicity; prediabetes; gateway to the cerebral circulation; leukæmia, viruses and radiation; hormonal genesis of mammary cancer; theories of antibody production; the arterial pressure pulse; aspects of climatic physiology; maintenance of hereditary defects and diseases in human populations; and chemical protectors against ionizing radiation. A new series of evening film sessions dealing with the film as a scientific teaching and research instrument was arranged. Besides a guest symposium on the definition and classification of pulmonary emphysema, several international conferences were arranged dealing with water and electrolyte mechanism in relation to age and sex; amino-acids and peptides with antimetabolic and cytotoxic properties; the recent contribution of medical biology to ethnology, with special reference to the origin of the Etruscans; the biosynthesis of terpenes and sterols; carcinogenesis: mechanisms of action; and the regulation of cell metabolism. Nine awards were made for research relevant to the problems of ageing and six British and four French candidates were awarded short-term Anglo–French exchange bursaries. Six volumes of conference proceedings were published, and besides details of the Foundation's research forums the report includes a list of publications.

Soviet Physics—Solid State

AN important new U.S.S.R. Academy of Sciences journal made its initial appearance last January, *Fizika Tverdogo Tela*. Offering results of theoretical and experimental investigations in the physics of semiconductors, dielectrics, and on applied physics associated with these problems, this periodical publishes papers on electronic processes taking place in the interior and on the surface of solids. The American Institute of Physics has added this monthly publication to the list of Russian physics periodicals now available in cover-to-cover translation. The English language version is called *Soviet Physics—Solid State*. Further information can be obtained from the American Institute of Physics, 335 East 45 Street, New York, 17.

School Natural History Societies

The contributions made by school societies to the spread of knowledge of their own areas is shown in booklets published by the Rugby School Natural History Society and the Biology Department at Stowe School. From Rugby comes a report of the activities during 1958 and, besides details of the work of various sections during the year, includes records of Cladocera which have been made by H. R. T. Price, and Syrphidae compiled by R. H. T. Tracy and J. Peirson. Stowe has produced "An Account of the Birds of Stowe", with records of the eighty-two species which now belong to the Stowe list. Articles on particular groups of birds which are found locally have either been taken from earlier issues of the school journal or have been specially prepared. Special tribute is paid to a former master, F. P. G. Aldrich-Blake, who appears not only to have inspired his boys but also the publication of this booklet in his honour.

The Manchester Museum

The first annual report for 1957–58 by Dr. D. E. Owen, the newly appointed director of the Manchester Museum (pp. 20. Manchester: The Manchester Museum, The University, 1959), reports progress in several directions. A gallery has been set apart for special temporary exhibitions, the policy to improve the display cases throughout the Museum has been accelerated and a new guide-book has been published. A bequest of Japanese material, including lacquer, ivory and bronze and collections of coleoptera and lepidoptera, has been received from the late Mr. R. W. Lloyd. A further bequest of similar importance was the Raby collection of coins. Popular lectures on Saturday afternoons attract an average audience of sixty-one, but an experimental series on Thursday evenings was not so successful. Members of the staff continue to carry out research on the collections, and an impressive list of publications is included in the report.

Work at the Royal Society Base, Halley Bay

The United Kingdom Antarctic Report to the fifth meeting of the Special Committee for the International Geophysical Year held in Moscow in 1958 (pp. 20. The Royal Society, 1958) includes a brief summary of matters from May 31, 1957, to May 31, 1958, dealing mainly with the work attempted at the Royal Society Base, Halley Bay. This included observations of meteorology (surface and upper air), geomagnetism, aurora, ionospheric measurements, and seismology. Over 1,250 upper air balloons were launched, some reaching heights of 20 km., during April and May. The heights during most of the dark season were much below expectation, but increased with the return of the sun above the horizon. There were many instrumental difficulties resulting from the harsh environment but for the most part these were overcome. Tables of provisional climatic data reveal that the highest daily maxima temperatures ranged from + 2° C. recorded in January (the only month recording a temperature above freezing-point) to − 15° C. in August. The lowest daily minima ranged from − 51° C. in July to − 15° C. in December. Snow fell on 191 days during the year. The visual and all-sky camera auroral data have been compared with those in the northern hemisphere during the period of the equinoxes in an attempt to find if any simultaneous data are available. The ionospheric data have shown that the diurnal variation of the *F* layer over Halley Bay is mainly determined by movements of ionization and not by the primary photo-ionization processes. Radio echo data obtained from auroræ have been compared with similar data from Jodrell Bank, and it is concluded that the great auroræ of the northern hemisphere are accompanied simultaneously by greatly enhanced activity of the aurora australis.

The glaciological data involved observations of the ice shelf, several hundreds of feet in thickness and partially aground, on which the station was located. The work included measurements of accumulation and ablation, and the temperature gradient within the ice, also the determination of past variations in the net accumulations. There were also frequent recordings of small seismic shocks that have been interpreted as occurring within a few degrees of Halley Bay.

Scientific Research in Central Africa

The attractively produced and illustrated ninth annual report of the Institute for Scientific Research in Central Africa covers the year 1956 (pp. 340. Bruxelles: Institut pour le Recherche Scientifiques en Afrique Centrale, 1958) and is in three parts. The administrative report includes particulars of the management and scientific committee, the financial statement and the director's report. The second part describes the opening of the Institute's main centre at Lwiro and includes the texts of addresses on the scientific work of the Institute and other research projects relating to central Africa. The third part comprises brief summaries of the work of the Institute during the year and a list of publications by the staff of the Institute or associated workers, comprising 145 titles. Abstracts of some of these are included. In his report as director, Prof. van den Berghe refers to the completion of a study of the tsetse flies of Mutara and Ruanda-Urundi, to studies of the biology of certain noxious rodents of Kivu, of the birds of the Tshibati region and their habitats and seasons of reproduction, and on the biology of the fish of Lake Tanganyika and of its coastal fauna. Observations on the forest ecology of Mabali and the borders of Lake Tumba and the collection of a herbarium continued, as well as inquiries into the migration of natives of Ruanda-Urundi into East Africa and into the agricultural economy of Ruanda-Urundi.

Oospore Germination in *Albugo candida*

Anton de Bary's well-known illustration of oospore germination in *Albugo candida* (published in 1863), in which a sessile vesicular zoosporangium is depicted, has long held its place in standard text-books. According to T. C. Vanterpool (*Can. J. Bot.*, 37, No. 2; 1959), no other investigation on this phenomenon in *A. candida* has ever been published. He has now demonstrated that if oospores, in hypertrophied inflorescences of rape (*Brassica napus* L. var. *annua* Koch), are kept in a refrigerator for 21 months, liberated from the tissue by grinding, soaked for 7–10 days in water at 10–12° C., then changed to fresh water, they will germinate. Moreover, he has shown that a second type of zoosporangium formation exists, namely, that on the rupture of the epispore, an exit tube, 1–2·5 times the diameter of the oospore, first grows out, the zoosporangial vesicle being then formed distally. The sessile type of germination, obtained under the same circumstances, was, however, the more common. Other interesting biological observations are also noted.

Trilinear Chart of Nuclides

The enormous amount of scientific data coming from laboratories of many countries is useless unless the information reaches the user as quickly as possible, and it must be in a form convenient enough to become popular with the searcher of information. In the case of the basic properties of nuclei large tables have been very useful, the most widely spread design being that due to W. H. Sullivan, which is based on a trilinear chart. In view of the continuous increase of information and the constant improvement of data already known, the sponsor of Sullivan's tables, the U.S. Atomic Energy Commission, is now offering a service to keep the collection up to date. This is done by replacing the hexagons making up the table with new ones containing the improved information. The first two sheets of replacements contain 45 and 49 hexagons, respectively, ready to be stuck over the old ones. The data reported are: isotopes, isobars, isotones, isodiapheres, beta line of stability, atomic mass, isotopic abundance, alpha and beta stability or instability, genetic relationships, production modes, disintegration modes, nuclear isomerism, radiation energy and intensity, half-life, branching ratios, per cent internal conversion, fission yield, whole element and isotopic cross-sections, spin, magnetic moment, and degree of certainty of A and Z assignment. The issue runs to 25,000 prints. Revision sheets can be obtained on a subscription basis from the Superintendent of Documents, U.S. Government Printing Office, Washington 25, D.C.

The International Academy of Management

At a recent meeting in Athens of the Executive Committee of the International Committee for Scientific Management, Mr. John Ryan, vice-chairman of the British Institute of Management, chairman of its International and Information and Research Committees, and vice-chairman of Metal Box Co., Ltd., was one of the eight new Fellows elected to the International Academy of Management. Nominees for membership were submitted from the twenty-nine countries of the International Committee and, among others elected, were Gaston Berger of France, Peter F. Drucker of the United States, Hugo de Haan of Austria, Bernhard Hellern of Norway, Theodore Limperg of Holland, E. Hans Mahler of Switzerland and Harold B. Maynard of the United States. The Academy was created by the International Committee in November 1958, for the purpose of "stimulating and honouring distinguished personalities for their contributions to the field of scientific management". One of the first activities of the Academy will be the selection of a prize paper to be read at the twelfth World Congress on Management being held in Australia during February 22–March 4, 1960.

Symposium on Geochemistry

A symposium on geochemistry organized by the Commission on Geochemistry of the International Union of Pure and Applied Chemistry will be held in Göttingen, Germany, on August 21 and 22, to be followed by two days field excursions. The topics for discussion at the Symposium are: stable nuclides in geochemistry; long-lived radionuclides in natural systems; geochemistry of the halogens; geochemical aspects of life on earth. Further information can be obtained from Prof. C. W. Correns, Sediment-Petrographisches Institut, Göttingen, Lotzestrasse 13.

Announcements

Dr. J. S. Anderson, professor of inorganic and physical chemistry in the University of Melbourne, has been appointed director of the National Chemical Laboratory, Teddington, in succession to Dr. D. D. Pratt, who is retiring.

The Dr. W. S. Bruce Memorial Prize for 1958, commemorating Dr. W. S. Bruce, the Scottish explorer and scientific investigator in polar regions, has been awarded to Dr. Hal Lister, Department of Geography, King's College, Newcastle upon Tyne, for his glaciological work with the 1957–58 Trans-antarctic Expedition. The committee of award is appointed by the Royal Physical Society of Edinburgh, the Royal Scottish Geographical Society and the Royal Society of Edinburgh.

Messrs. Pfizer, Ltd., the Kent manufacturing chemists, have awarded a university scholarship for science worth £370 per annum to Miss Penny Howard, of Abingdon, Berkshire, and one for chemistry worth £465 per annum to George Sayce, of Hampton Hill, Middlesex.

The Plant Phenolics Group is to hold an International Symposium on "Humic Acid" in the Department of Chemistry, University College, Dublin, on September 10 and 11. Further information can be obtained from the honorary secretary, Dr. T. Swain, Low Temperature Research Station, Downing Street, Cambridge.

A Conference on Ion Exchange will be held at the Mountain View Hotel, Gatlinburg, Tennessee, during September 7–11, under the sponsorship of the Oak Ridge National Laboratory. Further information can be obtained from Wm. Rieman, III, Ralph G. Wright Laboratory, Rutgers, The State University, New Brunswick, New Jersey.

The annual meeting of the Electron Microscope Society of America will be held during September 9–12 in Columbus, Ohio, at the Ohio State University, when a symposium is to be arranged on "Contribution of Electron Microscopy of Viruses and Cells to the Problem of Cancer". Further information can be obtained from the secretary of the Society, D. Maxwell Teague, Chrysler Corporation, P.O. Box 1118, Detroit 31, Michigan.

Commission I of the International Institute of Refrigeration will be holding a conference in Copenhagen during August 19–26 as part of the Tenth International Congress of Refrigeration. The following topics will be discussed: applications of low-temperature techniques in nuclear physics; mechanical properties of metals at low temperatures; thermometry; industrial problems in connexion with the liquefaction and distillation of gases; equation of state of mixtures; fluids under high pressure; transport phenomena in gases, liquids and solids; other problems of the application of very low temperatures in industry. Further information can be obtained from Prof. A. Van Itterbeek, Naamsestraat 73, Louvain, Belgium.

Erratum. In the article entitled "Reaction of some Silicates with Chelating Agents", by Dr. D. A. Sutton, M. D. Middleton and R. A. F. Body, published in *Nature* of January 10, p. 99, in Fig. 1 "Process 1" should read "Process 2" and *vice versa*.

STEREOPHONIC SOUND RECORDING, REPRODUCTION AND BROADCASTING

IT is commonly remarked, with much truth, that engineering is impatient of scientific understanding ; history can cite repeated instances of engineering enterprise plunging ahead and producing devices of great efficiency and utility, which only afterwards have been blessed by scientific theory when this has shown them to have reached near-theoretical limits. For this, the engineer needs no apology. His first concern is not analysis but synthesis ; his purpose is a social one, and he must for ever be content with compromise, drawing upon such science as may exist, using judgment and even guesswork to satisfy his customers.

This has been true of most branches of the electronics industry ; radio, radar, television and now 'hi-fi' and stereophony are triumphs not primarily of science but of technology.

Stereophonic recording, reproduction and broadcasting, the subject of a Convention held under the auspices of the Institution of Electrical Engineers on March 19 and 20, represents one of the latest catchpurses to tickle the public fancy. Such conceits spread quickly, perhaps we might unkindly say, first among those who lust after the latest gadgets ; but if this newest branch of the radio and gramophone industry is thus encouraged, there is no doubt that musical education will also benefit eventually. But the practical systems of stereophony are as yet imperfect, and there is room for ingenuity and inventiveness—and, in my opinion, more room now for science.

This was perhaps the most disappointing aspect of the Convention, that it was concerned almost entirely with techniques ; with practical problems of recording head design, with standardizing the grooves in gramophone records, with magnetic-tape machine design for easy operation and low cost, with techniques of compatibility whereby stereophonic (twin-track) signals may be used by those unfortunates who possess conventional one-loudspeaker sets—but almost nothing was heard concerning the theoretical basis of stereophony, nor of the unsolved problem of binaural hearing. For we still do not fully understand directional hearing, either psychologically or physiologically.

The opening paper, by Mr. T. Somerville, rightly emphasized the pioneer work of Blumlein, some thirty years ago. Blumlein's name is specially associated with systems of stereophony which use coincident microphones ; these are not spaced apart in the studio, but have their directional characteristics angularly spaced, such that a sound reaching them sets up two signals with different amplitudes.

It would have helped the Convention if, at this early stage, some explanation of the essential theory of stereophonic hearing had been presented—aided by simple geometric diagrams. In this way we might have avoided several confusions which arose later. For example, simple geometry readily shows how, in Blumlein-type systems, the *amplitude*-difference at the two microphones becomes converted into a *time*-difference between the two ears of a listener at the receiving end. Of course, our sense of direction does not entirely depend upon the binaural time-interval but upon other sensory clues as well—but it is very important.

Mr. F. H. Brittain, who followed with a paper comparing normal directional hearing with that provided by the twin loudspeakers of stereophony systems, valiantly tried to clear up certain misconceptions. Thus he stressed that the signal from any one microphone in the studio, fed to one loudspeaker in your living-room, reaches both your ears. The facts that you have two ears and that usually two microphones are used are not related—the microphones do not in any sense "simulate your two ears" (one later speaker had the good grace to apologize for a slide, which showed a symbolic human head wrongly placed between two spaced microphones). Again, Mr. Brittain pointed out the distinction between *inter-aural* time-intervals (maximum, about 500 microseconds in normal conditions) and *intersource*, loud-speaker, time intervals (which may be several milliseconds). It is only the latter interval which concerns the so-called 'Haas effect', an effect which is of some importance for off-axis listening in stereophony. Thus if you sit well to one side of the room, the sound from one loudspeaker may reach both your ears 4–5 milliseconds before the sounds from the other ; in such circumstances, the sounds at each ear may fail to fuse, subjectively, and the illusion of spatial distribution is shattered.

In normal life our sense of sound direction arises from several acoustic clues ; in particular, differences in inter-aural time, intensity and in minor sound structure. But such differences alone cannot give an image outside the head—they produce right/left shifts only. We need, further, the variations of these differences with head turning (aural-kinæsthetic association). The only detailed references to these basic facts were made by Mr. Brittain, who outlined the difficulties involved in producing these desired inter-aural characteristics in the sound field from two spaced loudspeakers. He stressed that, ideally, we need loudspeakers with directional lobe-patterns of a special shape and which vary with frequency ; further, it would greatly help if the time-delay of sounds emitted from each loudspeaker could be varied suitably with angle. We could well have profited by a good deal more physical and psychological background to this Convention.

The remaining papers were technical. One by Mr. G. F. Dutton and another by Messrs. A. D. Burt and D. R. Andrews were concerned with magnetic tape recording. The first outlined the commercial possibilities of 7½ in./sec. tape records and reproducers, which now can be operated by people who are not mechanically minded. Tape records can be made with wide frequency-bands, with negligible 'print-through' between layers when stored and, most important, very low 'cross-talk' between the adjacent tracks of the two channels. This latter point was much discussed, and clearly it is a troublesome aspect of technique.

Mr. Dutton also outlined the problems of reducing the cost of stereophony on tape records, which relate to the use of slower speeds, involving better head resolution, smoother tapes and narrower tracks.

Very similar points were raised by the authors of the second paper, who dealt specially with the head design and with easily handled, quick-change tape 'cartridges'.

The final paper on the first day of the Convention, presented by Mr. J. Moir, discussed cinema stereophony. It is characteristic of cinema systems that they have used 3, 4, 5 or even 6 loudspeakers, as opposed to the usual pair of domestic systems. Now with two microphones, only two-point samples of a continuous sound field in the studio are taken, so that the two spaced loudspeakers in your living-room set up a kind of diffraction pattern; this is perhaps more or less correct if you sit in the middle, but not if you sit to one side. Cinema audiences, however, occupy a wide angle, giving corresponding difficulties. One might have hoped that this greater number of spaced microphones would be used to give a more accurate simulation of the studio sound field, but Mr. Moir pointed out that studio personnel have not, in the main, understood the true problem. Most film recordings have used single-track technique, merely switching the sound image about the screen to be roughly coincident with the photographic image, by potentiometer control of the recording level from each microphone: a difficult proceeding if two actors speak simultaneously.

An evening session was devoted to broadcast stereophony. Mr. D. E. L. Shorter stressed the difficulties of 'compatibility'—conventional one-channel reception of an intended stereophony broadcast—and the technical difficulties of modulating a single carrier wave by two sources. Dr. W. S. Percival described an ingenious stereophonic system in which the two channels convey (*a*) the main acoustic content, (*b*) the acoustic direction clues, the latter requiring very low information rates indeed; he quite rightly observed that our sense of direction is most sensitive to transient sounds, and his system takes maximum notice of these.

Two papers were delivered on the second day dealing with disk recording. Mr. Dutton referred to internationally agreed standards, both of cutting and pick-up techniques. The most-favoured system, called the 45/45 system, uses orthogonally placed needles at 45° to the vertical. For best performance, minimum wear, cross-talk, etc., fully mechanical standards have now been set up. Great attention is also being paid to improvements in cutter and pick-up design, for better reproduction and easier manufacture, a topic dealt with in some detail by later speakers.

The Convention closed with a lively discussion, admirably refereed by Mr. Moir, which provided as much interest as some of the main proceedings. Perhaps the Institution of Electrical Engineers can be persuaded to present another Convention later, dealing with principles and fundamental problems rather than so much with design of apparatus. Engineers have gone a long way in this field on inadequate theory, or on none at all. This Convention showed the need now to be pressing.

COLIN CHERRY

INDUSTRIAL PHOTOGRAPHIC AND TELEVISION EXHIBITION

THE Industrial Photographic and Television Exhibition, which was held at the Royal Albert Hall during April 20–24, was sponsored and organized by the *Financial Times*. It was stated that "the object of the exhibition was to show executives the way in which photography can aid them in many stages of the industrial process or commercial activities".

Throughout the duration of the exhibition a number of lectures were given each day on the use of photography and television in the factory, the office, training and advertising.

The most obvious use of photography is its ability to record events for future reference. A photograph can store, in one instant of time, much more information than an observer could absorb—information the importance of which may not even be appreciated at the time. Such records can be examined in detail and at leisure at a later date. They can also be compared with others taken at different times, in order to find similarities and differences, as in astronomy.

In addition, photography can extend the field of human observation. If an event lasts only a fraction of a second, high-speed photography can be used to slow the action down. On the other hand, some changes are difficult to follow because they occur so slowly. By using time-lapse photography, the time-scale can be compressed and the whole cycle of action presented in a few minutes or less.

Furthermore, sensitized photographic materials are sensitive to many forms of radiation to which the eye does not respond in a useful manner, such as infra-red and ultra-violet radiation, α-, β-, γ- and X-rays and atomic particles.

X- and γ-rays are used in radiography, which is a non-destructive method of examining the internal structure of a wide range of objects, including human beings. From X-ray and electron diffraction patterns information can be obtained about the fine structure of materials, and in the electron microscope the use of an electron beam enables greater resolution to be obtained than with the optical microscope.

Special emulsions have been developed to help the nuclear physicist record the tracks of particles such as electrons, protons, mesons, etc., moving at high speeds. From these records he gains knowledge of atomic and nuclear structure.

The most striking feature of the exhibition was a large display of excellent black-and-white and coloured prints illustrating the uses to which photography could be put in industry, research, documentation and advertising.

Among these was a set of prints taken by reflected polarized light showing the growth of magnetic domains on the surface of a metal with increasing magnetic field (International Computers and Tabulators, Ltd.).

Examples of high-speed photography included a study of spray formation from high-pressure jets (Babcock and Wilcox, Ltd., and John Thornycroft, Ltd.). Another series of photographs illustrated a method of demonstrating fluid-flow by recording the paths taken by numerous small air bubbles suspended in a liquid. The apparatus was illuminated from one side by a flash bulb through a narrow slit so that a thin lamina perpendicular to the camera axis was photographed (Harold White, for the Power Gas Corporation, Ltd.). The Bowater Paper Corporation, Ltd., exhibited a print taken at 1/8000th of a second showing the fluid pulp on the wire mesh of a paper-making machine.

Other pictures showed the use of enamel for revealing the pattern of strain in metals (A. V. Roe, Ltd.), photoelastic stress patterns in gears and pawls (International Computers and Tabulators, Ltd.), the ultrasonic testing of metals (Steel Co. of Wales) and recording of cracks in concrete (Babcock and Wilcox, Ltd.). The last firm also showed photomicrographs of metal structure.

Probably the stand which was best arranged to enlighten the hypothetical executive was that of Pye, Ltd. It was divided into a series of cubicles, each one of which showed an application of closed-circuit television, such as the transmission of printed information or instrument dial readings or the examination of machinery in operation in inaccessible or inconvenient positions. Details were also given of a special camera designed to operate inside a nuclear reactor. Similar equipment was also exhibited by Marconi Wireless Telegraph Co., Ltd., for traffic observation and control.

Rank Cintel, Ltd., were demonstrating a three-channel colour-television apparatus and a video tape recorder. They also showed how television techniques could be applied to photographic printers and enlargers to adjust the contrast of a negative to improve print quality.

Decca, Ltd., showed a data-transmitting system which used a cathode-ray tube as a scanner with a photomultiplier pick-up tube.

The three photographic firms who exhibited featured document copying and reproduction. Gevaert, Ltd., showed examples of the 'Gevacopy' process which utilizes silver image transfer for producing a few copies. If a larger number are required then an offset printing plate on aluminium can be prepared. Ilford, Ltd., demonstrated a range of machines for using 'Azoflex' paper. This is a dye-coupling process which is capable of producing either as small or as large a number of copies as needed. On the Kodak stand was to be found the 'Verifax' process. This uses a layer which is hardened by light and afterwards pigmented. Any unhardened gelatine on the 'negative' can be transferred, more than once, to other sheets of paper to obtain several copies. Also shown on this stand were the 'Statfile' and 'Recordak' machines. A new model of the latter enables both sides of a sheet of printed material to be recorded side by side on a strip of film in one passage through the machine.

These firms also showed examples of radiography, colour transparencies and prints, etc., illustrating their uses in various fields. Ilford, Ltd., had a compact processing unit for 35, 45, 60 and 70 mm. film, which should be very useful to laboratories which employ oscillograph recorders, etc.

On other stands a wide variety of photographic equipment and chemicals could be seen: cameras (still and ciné), lenses, lighting units, timers, printers, enlargers, etc. John Hadland and Co. offered a complete service for high-speed photography. Many stands offered projectors for still and ciné pictures, with and without a commentary in sound for instruction, sales promotion, demonstration and advertising.

R. J. Hercock

CHELSEA COLLEGE OF SCIENCE AND TECHNOLOGY

NEW BUILDING

A NEW wing was opened at Chelsea College of Science and Technology on April 28 by Lord Adrian. The building was planned a number of years ago before the status of the College was changed and is thus relatively small and does not allow for any increase in social amenities for the College. Plans for further buildings on adjacent sites which will provide residential and social accommodation as well as a completely new Department of Chemistry are already well advanced. A new independent College of Art is also to be built opposite the present College building. In due course the School of Art, which now forms part of the College, will occupy the new building and release accommodation which will be adapted for use by the remaining departments of the College.

The present extension, which provides an additional floor area of 17,913 sq. ft., takes the form of a four-story block running roughly from east to west and facing north to Chelsea Square, with a two-story addition facing inwards to the courtyard of the College. A gap on the second floor of the old West Wing has also been closed by the building of a new zoological laboratory and a smaller staff research laboratory. The main new building provides a laboratory, lecture room, and two store-rooms for physics, six classrooms, staff and office accommodation for mathematics, a large teaching laboratory, two research laboratories, a balance room and a lecture room for chemistry, and a studio, lithography room, store and students' rest room for art. A new students' common room is also provided, but this and the new Art School accommodation is merely exchanged for equivalent space vacated for use by the Department of Botany and Zoology and the College Library. Other rooms vacated by departments occupying the new wing will also be adapted for use by the School of Pharmacy and the Departments of Geology, Physiology and Pharmacology.

In introducing Lord Adrian, the chairman of the Governing Body, Mr. John Townsend, directed attention to the fact that the College was the only college of advanced technology which did not possess an engineering department and the only one which did possess a department of physiology. Lord Adrian referred to the important and expanding fields of training and research which come within the scope of the work of the College. While the need for many more trained engineers was well recognized, there was some danger of neglect of the biological side. Chelsea was well placed, with its large School of Pharmacy and its other science departments, to help in satisfying this need. He likened the present boom period for science to the time when Gresham College was founded in the City of London and the Royal Society began its existence. At that time there was no clear distinction between science and technology and many famous men exemplified the union of the two in their own work. The distinction began to be emphasized in the nineteenth century but now it was growing out of date again; advances could come from either direction—the demand for a prettier stocking might lead to new theories of molecular structure or the new theories might lead to new fabrics. He congratulated the students of the College on having chosen a scientific career at this exciting period of expansion and emphasized the great possibilities that lay before them.

After declaring the extensions open, Lord Adrian inspected the new buildings, and the whole of the College was thrown open to visitors.

N. M. H. LIGHTFOOT

ADMISSION OF STUDENTS TO UNIVERSITIES

ONE of the most notable contributions in the report* of the vice-chancellor of the University of Birmingham for 1958 is his account of admissions procedure. Students are chosen by the faculty admission tutors in consultation with the heads of departments. The process goes on from January every year (or earlier) until September. Applications come from all over Britain, and from overseas, in numbers far exceeding the available places. Many are from candidates simultaneously applying to other universities as well, often with a preference for Oxford or Cambridge. They furnish school records, and headmasters' and headmistresses' assessments; many of them are brought to the universities for interview. More often than not the crucial information about applicants, namely, their performance in the 'A' level examinations for the General Certificate of Education, is not available until mid-August, but it is impracticable to leave all decisions until that late date. Tentatively, at least, the university must make most of its choice before then, while the candidate also wants to exercise his choice among universities. The result is that a complicated and haphazard system of provisional offers of admission has grown up, in which the universities compete for what they think are good candidates and the candidates compete for what they think are good universities. The universities often keep the candidates on tenterhooks and the candidates sometimes treat the universities in cavalier fashion.

The position has grown worse in the past three years, and threatens to grow worse still as numbers and competition increase. No smooth and tidy system seems possible so long as General Certificate examinations are held in June and university sessions begin in October; if those events were to be separated by a longer interval of time, no one can think how to occupy the boys and girls during that interval, short of imposing some kind of civilian national service. In studying the difficulty, however, the Committee of Vice-Chancellors and Principals concluded that it could at least be mitigated, and in June 1958 the Committee made a series of recommendations to the universities (other than Oxford and Cambridge) designed to smooth the path of university applicants to a considerable extent. It asked, among other things, that application forms should be simplified and made more nearly uniform; that heads of schools should be invited to use a common form for reports on candidates; that application and acceptance fees, and special entrance examinations, should be abolished; that closing dates for the receipt of normal applications by all universities should be synchronized; that provisional offers of places should state the conditions in specific terms; that candidates should be informed as promptly as possible where they stand, and be allowed reasonable time in which to accept or decline places offered to them. Birmingham has accepted these recommendations and is giving effect to them in 1959. If all universities do the same there is likely to be a substantial improvement in an inherently difficult situation.

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* University of Birmingham. Report of the Vice-Chancellor and Principal for the Calendar Year 1958. Pp. 26. (Birmingham: The University, 1959.)

DIRECTORY OF NATURAL HISTORY AND OTHER FIELD STUDIES

ON behalf of the Carnegie United Kingdom Trust, the British Association for the Advancement of Science has performed a useful service to many people in compiling a directory of natural history and other field societies.

The response to 4,000 individual inquiries made by Dr. Averil Lysaght showed that some eight hundred natural history societies flourish in Great Britain to-day. These he carefully listed and provided with a geographical index so that their work may be better known and co-ordination between them facilitated.

The publication of the Directory, so shortly after the formation of the Council for Nature, reflects the increased interest in natural history. As a comprehensive work of reference, it has attempted to include all professional and amateur societies in England, Scotland, Wales and Northern Ireland which are concerned in any way with field studies (a term which provides an umbrella for a multitude of subjects from interplanetary exploration to guppy-breeding), or which, while not taking part in field work themselves, are active in publishing the results of such work. Medical societies have not been included, nor have societies devoted to horticulture, agriculture and forestry, nor those concerned with plants or animals purely for sporting or commercial purposes. School societies have only been listed if they publish some record of their work or carry out some special studies; it is impressive to note how many do fulfil these qualifications.

Of the societies listed, those which claim to be specifically concerned with natural history and field studies form the majority, with archæology and local history making a close second. A considerable number—somewhere about 10 per cent—are occupied with the preservation of the countryside in the broadest sense. Astronomy and meteorology are combined in a single section; geology has a section to itself, though many geologists must be numbered among the members of the geographical societies listed in the general section. Bird-watching and ornithology prove the most popular single subject, and the Directory reflects the growth of new types of society, such as the various spelæological societies engaged in surveying and excavating cave systems in Great Britain; the underwater swimming clubs, many of which are turning from sporting and hunting activities to the study of freshwater and marine life, as well as the development over recent years of the county naturalists' trusts.

There is a strongly local flavour to a high proportion of the societies. Life membership thrives in Scotland and diminishes with decreasing latitude; after London, Yorkshire boasts the largest concentration of societies; Lincolnshire can claim the second oldest in England (ranking next to the Royal Society), which numbered among its members Newton, Addison and Pope. Glamorgan holds the monopoly in the study of lichens, while underwater swimmers are as bold in the north and midlands as in the south. The geographical index provides an easy guide to the regional distribution.

PROPERTIES OF A RECEPTOR MEMBRANE

From THE DEPARTMENT OF PHYSIOLOGY, COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIANS AND SURGEONS, NEW YORK

Spatial Summation of Electric Activity in a Non-myelinated Nerve Ending

After removal of most of the non-nervous (capsular) tissue of a Pacinian corpuscle, the sense organ's remains, consisting mainly of a non-myelinated ending, continue to be as mechano-sensitive as the intact sense organ: the ending produces generator potentials in response to mechanical stimuli of the same order of magnitude as the intact corpuscle[1]. This decapsulated preparation offers the opportunity to study the properties of a non-myelinated nerve ending in isolation. The ending is accessible for micro-electrode recording, and visually selected portions of ending can be stimulated mechanically with a crystal-driven stylus. The ending is straight and long (about 600μ); two separate regions of ending can be stimulated simultaneously with two independently driven styli.

When a mechanical stimulus is applied to a portion of ending by one stylus alone, an active response (depolarization) is detected at that region. This response is confined to the region of ending which has been stimulated mechanically, but does not propagate actively along non-stimulated portions of ending. Fig. 1 illustrates an experiment in which two micro-electrodes are placed in contact with the ending. A weak mechanical stimulus is delivered to a portion of ending close to electrode E_1. This causes depolarization of a region of membrane in the vicinity of the stimulating stylus which is recorded by electrode E_1. Electrode E_2, about 500μ apart, still detects this response, but the peak amplitude and the rate of rise of the response are markedly reduced. By systematic scanning of the ending's surface with a micro-electrode, the amplitude of the response is found to decrease exponentially with the distance from the stimulated region.

From the preceding results spatial summation of electric activity of independently active membrane regions[2] emerges as a possible mechanism to account for the well-known increase in generator potential as a function of the strength of stimulus. It was, in fact, found that the depolarization of one membrane region adds up with the depolarization of another region. In the experiment illustrated in Fig. 2 the styli of two independent crystals were each applied to a

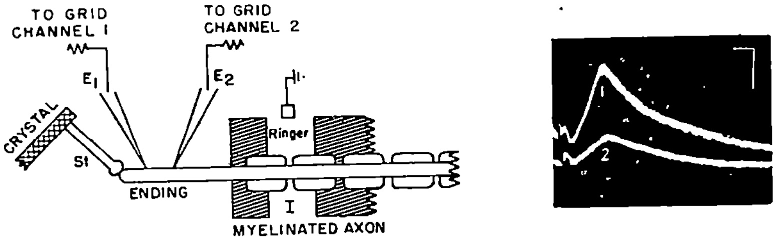

Fig. 1. Local activity confined to a small membrane portion of ending. Two micro-electrodes (E_1, E_2) connected to separate amplifier channels are placed in contact with the non-myelinated ending of a decapsulated Pacinian corpuscle. The preparation is pulled into a device which insulates the first node of Ranvier in contact with a common ground electrode from the ending. E_1 is placed at a distance of approximately 20μ, and E_2 at approximately 520μ distance from the stimulating stylus (*St*). Beams 1 and 2 give the responses to a single mechanical stimulus as recorded by electrodes E_1 and E_2, respectively. Calibration: 50 μV.; 1 msec.

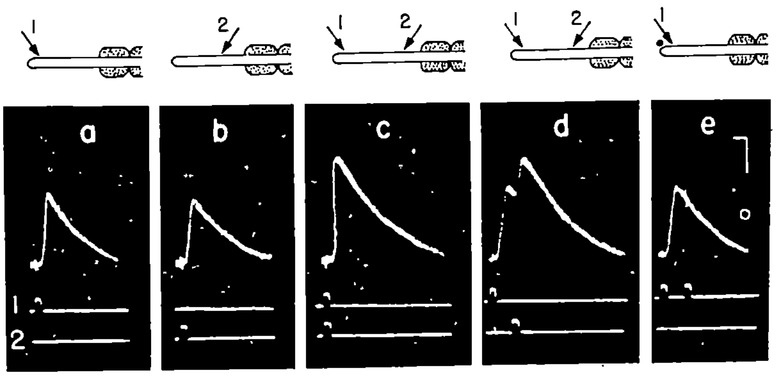

Fig. 2. Spatial summation of generator potentials in a single nerve ending. Styli 1 and 2 belong to independent stimulating crystals which deliver stimuli to two separate regions of ending. Middle and lower beams signal stimuli of styli 1 and 2, respectively. Upper beam for generator potentials as recorded at the myelinated axon. *a*, stylus 1 alone delivers one stimulus; *b*, stylus 2 alone delivers one stimulus; *c*, styli 1 and 2 deliver each one stimulus simultaneously; *d*, stylus 2 applies a stimulus 1 msec. delayed from that of stylus 1; *e*, stylus 1 alone delivers two stimuli succeeding each other at a delay of 1 msec. Calibration: 1 msec.; 50 μV.

different region of ending. The electric activity of the ending was led off by electrotonic spread from a myelinated portion of axon near to the ending with a pair of low-resistance electrodes. Such electrodes integrate current flow from the entire ending. When both styli deliver simultaneously a stimulus to their respective membrane regions, summation of electric activity is observed (Fig. 2 *c*, *d*.) The possibility of a mechanical artefact due to mechanical spread of stimuli or due to mechanical summation of stimuli is excluded by the result shown in Fig. 2*e* : if two successive stimuli, separated by the same interval as in *d*, are delivered to the *same* membrane region by one stylus alone, the second stimulus falls on the refractory trail of the preceding response[3] and fails to evoke a detectable response. This experiment in addition reveals that the refractory state (as well as excitation) is confined to that region of membrane which has been activated mechanically, but does not spread along the ending's membrane.

WERNER R. LOEWENSTEIN

Spontaneous Fluctuations in Generator Potential in a Receptor Membrane

THE receptor membrane of the non-myelinated ending of Pacinian corpuscles has the peculiarity that small regions of it can be activated independently ; as has just been shown, if a mechanical stimulus is applied to a portion of ending, the resulting active response (depolarization) is confined to that region which has been stimulated, but does not propagate actively to adjacent non-stimulated regions of the ending by local circuit excitation[2]. The generator potential of the entire ending appears to be the result of spatial summation of electric activity of functionally independent membrane regions of a certain minimal area[2]. The term 'receptor site' will be used here to designate that minimal region of membrane which can be activated independently. The term 'site' is used in its broadest sense. It does not imply structural discontinuity of the membrane ; it merely implies discontinuities in the process of activation along the ending's membrane. Evidence has recently been given indicating that a mechanical stimulus activates a statistically fluctuating population of receptor sites[4]. One of the consequences of this mode of excitation, the existence of spontaneous fluctuation in generator potential, has been explored in the experiments described under the second heading.

Isolated Pacinian corpuscles from the cat's mesentery were stimulated with mechanical pulses from a piezo-electric crystal. The pulses were monitored photoelectrically with an accuracy of 0·3 per cent. The ending's generator potential was led off with an electrode placed on the region where the non-myelinated ending joins the myelinated axon. Such an electrode records the aggregate electric activity (generator potential) of the entire receptor membrane.

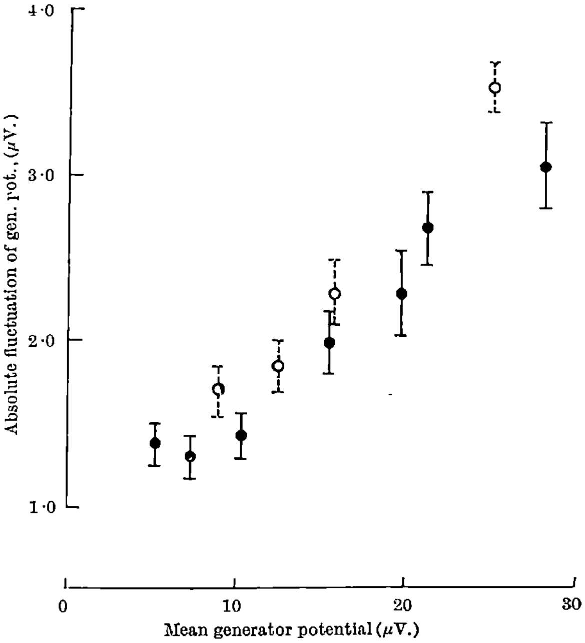

Fig. 3. Absolute fluctuation in generator potential as a function of amplitude of generator potential. Each point corresponds to the mean fluctuation (deviation) in amplitude of 50 generator potentials in response to equal mechanical stimuli ; bars subtend standard error of mean fluctuation. The mean amplitude of generator potential is varied in steps by either (*a*) varying the stimulus strength over the linear range of the stimulus strength–generator potential function ; or by (*b*) polarizing the non-myelinated nerve ending at constant stimulus strength. The mean fluctuations in generator potential obtained by procedure *a* (black circles) and by procedure *b* (open circles) are plotted against the mean amplitude of the corresponding generator potential

When equal mechanical stimuli are applied to the same portion of ending, the amplitude and rate of rise of the resulting generator potentials were found to fluctuate at random around an average value. Fig. 3 shows the fluctuations in amplitude for various amplitudes of generator potential. Each point of the curve corresponds to the mean fluctuation of 50 generator potentials produced by equal mechanical stimuli. The mean amplitude of generator potential was increased in steps by increasing the stimulus strength within the linear range of the generator potential–stimulus strength function, and the corresponding fluctuation of generator potentials (black circles) was determined for each strength. The fluctuation is seen to increase with amplitude of the generator potential. It has previously been shown that the area of activated receptor membrane, that is, the number of active sites, increases with strength of stimuli applied to the ending[2]. An increase in statistical fluctuation of active sites, and hence an increase in fluctuation of generator potential with increasing stimulus strength, such as observed in the experiment of Fig. 3, is thus to be expected. It might furthermore be expected that, as a consequence of spatial summation, the increase in number of activated sites with increasing stimulus strength be steeper than the corresponding increase in statistical fluctuations of active sites. The ratio of generator potential fluctuations to generator potential should then decrease with stimulus strength. It is apparent from Fig. 3, and further illustrated by Fig. 4, that this ratio, in fact, decreases with strength over the linear range of the generator potential–stimulus strength function. The results are thus in agreement with a system in which the generator potential is the result of spatial summation of activity of statistically fluctuating receptor sites. However, the possibility must be considered of the observed fluctuations being caused by fluctuations in mechanical stimuli. From the derivative of the stimulus strength–generator potential curve corresponding to the fluctuation curve of Fig. 3, it can be calculated that the mechanical stimuli would have to fluctuate as much as ± 4·7 per cent to account for the smallest value of observed fluctuation. However, the photoelectric control of stimuli gives us the certainty that

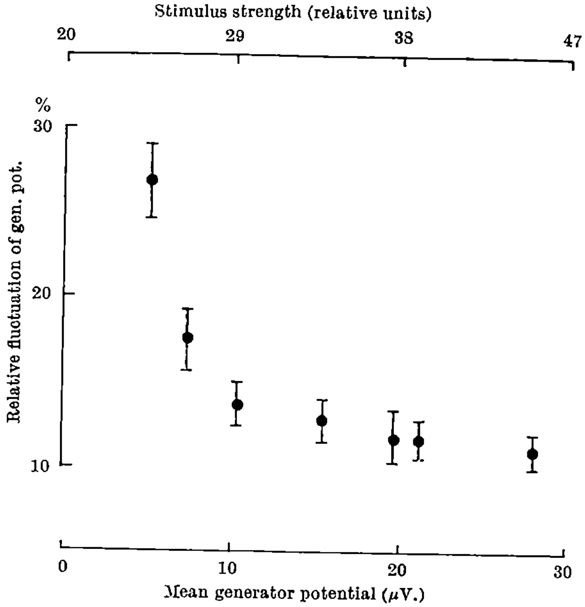

Fig. 4. Relative fluctuation of generator potential as a function of generator potential. The percentage fluctuation (100 × mean fluctuation/amplitude of generator potential) is plotted against the mean amplitude of generator potential. Data from the same ending as Fig. 3 obtained in the linear range of the generator potential–stimulus strength curve

stimulus fluctuations were below 0·3 per cent; possible contributions of stimulus fluctuations to the observed fluctuations in generator potential are, therefore, negligible. Another possibility had to be considered. The fluctuations of generator potential may have been caused by uncontrolled fluctuations in mechanical coupling between crystal stimulator and receptor membrane. If such fluctuations were to increase with stimulus strength, a similar result to that of Fig. 3 could conceivably have been produced.

The following experiment eliminates this possibility. The ending was stimulated with equal mechanical pulses, while its membrane potential was increased to various levels by inward flowing currents. The generator potential increases as a function of membrane potential. The fluctuations in generator potential could thus be studied over a range of generator potential without changing stimulus strength. The fluctuations were found to increase with amplitude of 'polarized' generator potentials (open circles) in the same manner as by increasing the stimulus strength (black circles, Fig. 3). Since under these conditions stimulus fluctuations remained unchanged, the observed increase in fluctuation of generator potential could not have been caused by an increase in fluctuation of mechanical coupling. An alternative possibility that constant fluctuations in mechanical coupling might be multiplied by a factor proportional to the amplitude of generator potential can also be dismissed: it would require that the fluctuation/generator potential ratio be constant instead of progressively diminishing as observed in the experiment of Fig. 4.

It may safely be stated, in conclusion, that the observed fluctuations in generator potential are due to spontaneous fluctuations of activity in the receptor membrane. It is interesting that the receptor membrane of a mechano-sensitive nerve ending resembles in this way the postsynaptic membrane of skeletal muscle, for which evidence has been given that electrical activity is built up statistically[5].

This work was aided by research grants from the U.S. National Science Foundation and the U.S. National Institutes of Health.

Nobusada Ishiko
Werner R. Loewenstein

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NOMENCLATURE AND CLASSIFICATION OF THE TEA PLANT

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THE relevance of taxonomic research to the principles of tea cultivation is not generally understood: this article, therefore, directs attention to taxonomic investigations in India and shows their applicability to crop studies.

Botanists describe the tea plant as *Camellia sinensis* (L.). The species was typified by Linnæus with an illustration from Kaempfer[1]. Occidental interest in more recondite classification probably began with Masters[2], who placed the forms now known as *C. sinensis* var. *assamica* (Masters) in a natural category with a distinct type; but he was uncertain whether the remaining forms could be referable to a single type.

Botanists have generally recognized two taxa at varietal level[3], defined largely by leaf-form: the China or type variety (*C. sinensis* var. *sinensis* L.) and the Assam variety (*C. sinensis* var. *assamica* Masters). Typically the China variety is a shrub with more or less virgate stems arising near the ground, 1·0–3·0 m. tall, with relatively small, hard, dark green leaves 3–6 cm. long, with a dull (matt) surface. Typically the Assam variety is a small much-branched tree 10–15 m. tall, sometimes with a trunk one-third its height, with supple light green leaves 15–20 cm. long, with a glossy surface. 'Typical' is in the sense of botanical types of two categories of variants not clearly separated by heredity, and not geographically isolated, these being the implications of varietal status. In practice this classification results in a distinctive Assam variety with a great assortment of forms remaining in the China variety.

The Assam variety is less hardy than the China variety but has bigger yield. Tea made from the two varieties differs fundamentally[4] and one tea cannot be substituted for the other. Subsidiary forms of the Assam variety with dark and light green leaves are cultivated: the dark form might sometimes be hardier, but both make identical tea.

Watt and Mann[5] were probably the first occidental writers to appreciate the need for categories smaller than those defined by botanical nomenclature. Variation of tea leaves is similar to the variation of *Ulmus* leaves. In tea, Watt and Mann described provisional categories of leaf-form within the Assam variety and associated them with regions in north-eastern India. They wondered whether their categories were "natural races or not". Number of leaf veins was emphasized; but this has not proved to be a satisfactory criterion.

Major geographical regions certainly differ in their characteristic tea populations in a way that has not been adequately described, but plants referable to all of Watt and Mann's categories might be found growing together as part of heterogeneous populations in many places; or any one might be found separately in some minor ecological niche on which its separation would depend. Nevertheless there is an unfounded tradition among tea planters that the regional names which Watt and Mann associated with provisional categories define scientifically acceptable types of tea: thus a misleading verbiage has been created, wrongly suggesting agronomically useful types called 'Burma', 'Lushai', 'Naga', 'Manipuri', and so on.

A valuable dissertation by Kingdon-Ward[6] includes the word '*cambodiensis*'. This cannot be accepted as a valid botanical name; but it was, and still is, used provisionally by me for the conceptual type of southern forms some aspects of which have been defined by Roberts, Wight and Wood[7].

Had arrangements been made for their reproduction, then Watt and Mann's leaf-forms could have been established as cultivars[8]. Vegetative propagation has not been practised. Seed is taken from perennial orchards each with a distinctive 'jat' name. Over many years similar, but internally mixed, populations are raised from one orchard: collectively they are known as a 'jat', and this could be regarded as a crude approximation to a cultivar; but one 'jat' might contain all the leaf-forms defined by Watt and Mann.

The naming of cultivars is a practical convenience, but the names can be unperceived obstacles to further knowledge: for example, variables like caffeine content and plant size become referable to names, thus giving relations in which names could, with advantage, be replaced by mathematical variables. Logical treatment of cultivar names is impossible unless they are arrayed in a definite order, and this can be achieved simply by replacing the names with a parameter characteristic of the plant: a suitable parameter would be an organ-frequency, such as number of special cells, or organs of some higher category. Research along these lines shows that the number of phloem parenchyma cells with druses of calcium oxalate in the leaf petiole of tea (conveniently called 'crystal frequency') enables individuals and populations to be placed on a genetically conditioned scale[9]. For simplicity, metrically defined progenies and groups of a crop-plant can be called 'agrotypes'[10]. In what follows attention is directed to the utility of agrotypes of tea defined by crystal frequency.

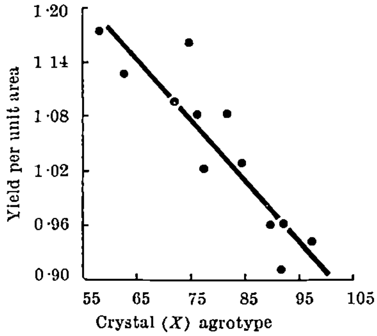

Fig. 1. Relation between the yield per unit area of tea bush and tea agrotypes defined by crystal frequency

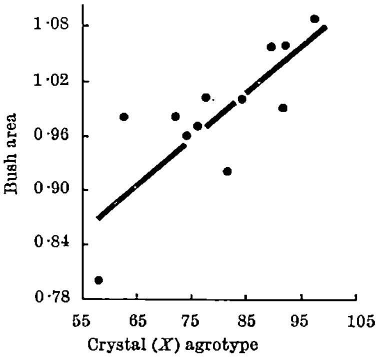

Fig. 2. Relation between the area of a tea bush and tea agrotypes defined by crystal frequency

In Fig. 1, the green weight (kgm.) of tea shoots plucked per square metre of bush surface per year is plotted against the (crystal) agrotype of 12 'jat' populations (cultivars) within the limits of var. *assamica*. Each point is the mean of 1,200 bushes equally divided between four cultural treatments. The correlation coefficient is $-0 \cdot 90$. The surface area of a bush in square metres is plotted against the same base in Fig. 2, the correlation coefficient being 0·78. It could evidently be useful to regard the yield and dimensions of the tea bush as functions of agrotype, and this concept could permit extensions of knowledge that might be impossible with a nomenclatural base of reference. Other definitions of agrotype might sometimes be more appropriate, but the examples suffice to show the utility of a metrical system of classification.

Intergrades between the Assam and the China variety of tea are well known. In practice, intergrades and putative hybrids of plants can be assigned to nomenclatural categories (taxa) by subjective judgment[12,13], showing that a 'specificness' can be recognized. The 'type' of a taxon may be supposed to have maximum specificness. These notions are illustrated by Fig. 3, in which *A* and *B* denote the types of var. *assamica* and var. *sinensis*: between them is an array of leaf-form intergrades (nine in the example) based on an aggregate of vegetative characters in the sense indicated by Li[11]. From *A* to *B* they look less like *A* and more like *B*. Observations which need not be described here show that the general trend of crystal frequency in such an array would be suggested by the column heights of Fig. 3. The array is a 'cline'[13] with special features: specificness different in kind diminishes from both *A* and *B* towards *O*, where it is supposed to be zero. Analogous clines of *Ulmus* were studied by Melville[14], but here another dimension is introduced in the form of crystal frequency. It follows from Fig. 3 that specificness of tea would be inversely related to crystal frequency.

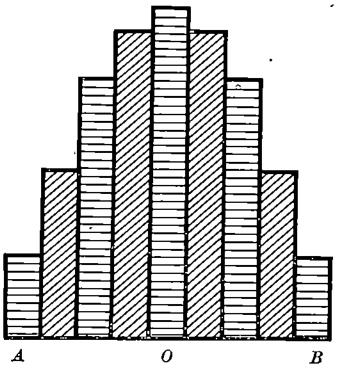

Fig. 3. Column heights indicate the expected trend of crystal-frequency along a cline of intergrades between tea taxa A and B

The 'nominal limits' of a taxon to which intergrades, putative hybrids and introgressants could be assigned might be from A or B to O, or just short of O; 'just short' often being a matter of personal judgment and anyway leaving indeterminate intergrades about O. With more than two taxa a manifold system of clines could be visualized.

While plants in var. *assamica* have typically glossy leaves, some matt plants occur in cultivated populations; but as integrated entities the populations could be within nominal limits of the taxon. Similarly, matt plants are typical of var. *sinensis* but many cultivated populations contain some glossy plants. Leaf-form agrotypes can be defined by the ratio of glossy to matt plants in a progeny population (G/M agrotype). This ratio should increase along the scale from B to A in Fig. 3. But, with O as origin, specificness increases in a positive and a negative direction, signifying two taxa: in one of them G/M would be a measure of specificness, and in the other M/G would be a measure of specificness. A relation between G/M and crystal frequency would be expected to differ in sign between the two taxa. Within nominal limits of a taxon, G/M agrotypes might approximate to a linear function of crystal agrotype, and investigation within the nominal limits of var. *assamica* (Fig. 4) has in fact shown that the two kinds of agrotype can be simply related to each other ($r = 0{\cdot}94$).

The taxonomic origin of tea made from the type variety can be recognized at once by a taster familiar with tea plants; and tea made from solitary matt-leaf plants, not necessarily referable to var. *sinensis*, is often described by tasters as 'chinary'. These observations suggested that some important attributes of tea might be determined by the specificness of the plant from which the tea is made; and this was confirmed by a significant second-order regression between the tasters' scores for 'quality' and the crystal frequency of the plants (unpublished). Thus both quality and yield can be associated with specificness, with the implication of important inter-relations between these three factors, and others such as pubescence[15].

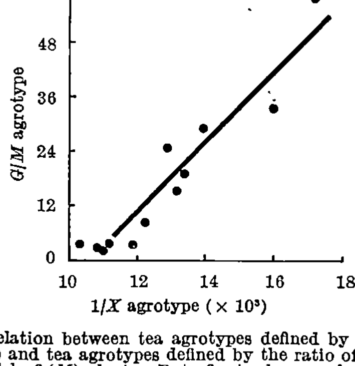

Fig. 4. Relation between tea agrotypes defined by crystal frequency (X) and tea agrotypes defined by the ratio of glossy-leaf (G) to matt-leaf (M) plants. Data for twelve populations within the nominal limits of var. *assamica*, showing that specificness (G/M) is a function of the reciprocal of crystal frequency ($1/X$). Each point is based on 400 bushes per population

Recently introduced mass selection[16], based on pubescence, is likely to alter the crop composition in north-east India; but so far large parts of the crop have approximated generally to crosses and back-crosses between var. *sinensis* and var. *assamica*. Some plantations have an origin in crosses between var. *assamica* and the introduced 'China' material discussed by Masters[2], part of which undoubtedly arose in species hybrids. Work at Tocklai has suggested three possible taxa within the Linnean species (*C. sinensis*) that could have contributed to the crop, and chemical investigations by Roberts *et al.*[7] show that the concept might be widely applicable: it would need to be related to the work of other taxonomists[3,18,19]. There is evidence for introgression from *C. irrawadiensis*[20,21]. Further work at Tocklai (unpublished) shows that each taxon indicated by Roberts *et al.* could be typified by a distinctive floral morphology; and crop surveys based on vegetative features show that the frequency distribution of intergrades between var. *assamica* and the type variety has discontinuities that would be inconsistent with mere varietal status of the two taxa. Although the recognition of taxa in which the crop may have originated is a theoretical necessity, it is to be remembered that taxa have no usefully distinct limits among crop populations: furthermore, there is no clear distinction between wild and cultivated tea[6]. The situation necessitates metrical classification, and it is possible for this to be complementary to botanical nomenclature.

While I am responsible for the point of view of the article, my ideas over several years have been clarified by discussions with Mr. P. H. Carpenter, Dr. E. K. Woodford, Dr. K. Biswas, Mr. J. R. Sealy, and Dr. G. Watts Padwick, whose interest and help it is a pleasure to acknowledge.

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LETTERS TO THE EDITORS

RADIATION BIOLOGY

Variation of Sensitivity to Ionizing Radiation with Age

The relation between the long-term effects of radiation and ageing has been the subject of much investigation in recent years, but little quantitative work has been done on the variation with age of the effects produced by a given dose of radiation. Using a single dose, Abrams[1] found a maximum mortality-rate in mice 4 weeks old. Hursh and Casarett[2] measured the *LD*50 in rats of different ages, and found a decrease with age in the latter period of life; somewhat similar results were obtained by Sacher[3] for mice. We are carrying out a systematic study[4] of the long-term effects of radiation in mice, with particular reference to the dependence of these effects on age. As part of this work, we have investigated the variation of sensitivity with age, using as a criterion of radiation damage the *LD*50 at 30 days.

The animals used were an inbred strain of albino mice (*SAS*/4), with a mean life of about 110 weeks. Except for the youngest age-groups, which were bred in our animal house, the mice were introduced into the colony at the age of 3 weeks. One week before irradiation they were divided randomly into cages of 8, the mice in every fifth cage serving as controls. About 400 mice—all of the same age—were used in each age-group, this number being divided into four dose groups of about 80 mice each, with the remaining 80 as controls. The numbers of males and females were about equal. When the mice reached the age for irradiation, they were given a single whole-body exposure of X-rays. The source of radiation was the 15-MeV. linear accelerator at St. Bartholomew's Hospital, and the dose-rate was about 400 r./min.

After exposure, the mice were returned to their cages, and deaths occurring during 30 days after the exposure were recorded daily. Regression lines of the mortality-rate versus dose were then plotted, using the method of probit analysis, and the *LD*50 values thus determined.

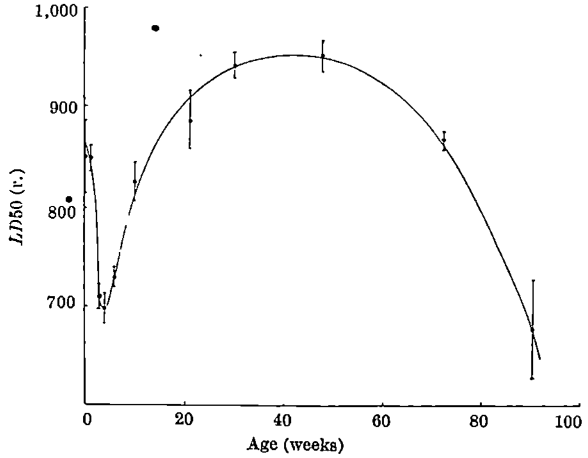

Fig. 1. *LD*50 for *SAS*/4 mice at 30 days as a function of age

Table 1 and Fig. 1 show the results obtained for mice over a range of ages from one day to ninety weeks. The standard error for each value of the *LD*50 is given in Table 1 and is indicated in Fig. 1 by vertical lines; it is about 2 per cent, except for the youngest and the oldest age-groups, where smaller numbers of animals were available. When comparing these results with those of other workers, note should be taken of the relative biological effectiveness of the 15-MeV. X-rays; in a separate experiment we have found that the relative biological effectiveness for our radiation, relative to 250 keV. X-rays, is 0·81.

Table 1. *LD*50 AND COEFFICIENT OF VARIATION FOR ALL MICE AS A FUNCTION OF AGE

Age (weeks)	*LD*50 (r.)	Coefficient of variation (per cent)
0·14	850 ± 37	11·9 ± 2·2
1	850 ± 13	9·6 ± 1·3
3	709 ± 13	19·4 ± 2·0
4	698 ± 16	25·2 ± 2·3
6	728 ± 10	15·5 ± 1·2
10	826 ± 20	18·8 ± 2·1
21	887 ± 30	15·2 ± 2·6
30	942 ± 13	13·7 ± 1·4
48	952 ± 15	14·9 ± 1·9
72	866 ± 9	12·2 ± 1·1
90	676 ± 50	31·0 ± 9·0

The median age at death decreased slightly with increasing dose (about 1 day/100 r.) but showed scarcely any variation with the age of the mice. For a dose equal to the *LD*50, the median age was 11·7 ± 0·8 days.

The *LD*50 values were also calculated separately for males and females and the results are given in Table 2. It is seen that although, in general, the variation of *LD*50 with age is the same for both sexes, there are some characteristic differences. The females appear to be slightly more sensitive to radiation when young, but after the age of 10 weeks they persistently show a greater resistance to radiation, the *LD*50 at a given age being about 50 r. greater than for the males. It is interesting that the expectation of life of females of this strain is about 4 weeks shorter than that of males.

Table 2. *LD*50 FOR MALE AND FEMALE MICE AS A FUNCTION OF AGE

Age (weeks)	Males (r.)	Females (r.)
3	702 ± 18	721 ± 16
4	708 ± 22	690 ± 22
6	748 ± 13	708 ± 12
10	863 ± 48	802 ± 16
21	861 ± 39	912 ± 51
30	907 ± 14	968 ± 27
48	935 ± 20	974 ± 27
72	855 ± 14	877 ± 11
90	641 ± 35	711 ± 50

Table 1 contains the coefficient of variation, that is, the standard deviation for each measurement divided by the *LD*50, which is a measure of the uniformity of the response. During most of life this coefficient varies very little. The high value at 90 weeks may be spurious, but the peak at about 4 weeks appears to be genuine, indicating a greater variability in the population at that age. This was confirmed by another observation. In our main experiment, on the long-term effects of radiation, we irradiated the mice at 4 weeks of age and we have obtained *LD*50 values at that age on several occasions during the past two years and for different batches of mice. The results show a considerable scatter in the *LD*50 values, ranging from 620 to 785 r. (the value given in Table 1 is the mean of these determinations). A similar experiment with older mice showed a very good reproducibility of the *LD*50 values. There was no epidemic or other cause to explain these findings, and we must thus conclude that at about 4 weeks, when the sensitivity of the mouse to radiation is highest, there is also a large degree of variability. This is one week after weaning, and so is a period of adaptation to a different diet and environment.

Our results clearly show that there is a considerable variation of sensitivity to radiation with age throughout life, but particularly so at a young age. None of the theories which have been put forward to explain the effects of radiation accounts for this variation. Blair's[5] theory predicts a steady decrease of the *LD*50 with age, proportionately to the remaining expectation of life. The last part of the curve of Fig. 1 does indeed follow the trend of the expectation of life curve, but it is clear that at younger ages there appears to be another intrinsic factor, which affects the sensitivity to radiation. Experiments aimed at elucidating the nature of this factor are now in progress.

Although it is imprudent to extrapolate from mice to men, and from acute to long-term effects, the variation of radiosensitivity with age observed by us may be a general effect, and in that event it may have to be taken into account both in radiotherapy and in setting maximum permissible doses.

We are indebted to the Nuffield Foundation and to the Endowment Fund of St. Bartholomew's Hospital for generous grants which made this work possible.

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PHYSIOLOGY

Contraction and Relaxation in Smooth Muscles of Lamellibranch Molluscs

MUSCLES such as the smooth adductors of lamellibranch molluscs maintain a state of tonic contraction with very little expenditure of energy, because normally tension persists long after stimulation has ended and the active state has decayed to zero[1]. As determined by the quick-release method[2], the intensity of the active state at any instant is indicated by the isometric tension the muscle can re-develop at that instant. The tension present after the active state has decayed to zero may be called passive tension. (The latter can readily be distinguished from resting tension, which only appears when the muscle has been stretched beyond the length it can assume in the animal's body[3].)

We have found that in a twitch response of the anterior byssus retractor muscle of *Mytilus*, the decay of tension can be two orders of magnitude slower than that of the active state, and this also applies when the active state is prolonged by stimulating the muscle for several seconds either with direct current or with acetylcholine[4]. From experiments with a variety of molluscan muscles, but particularly with the anterior byssus retractor muscle of *Mytilus* (all of which contain filaments showing paramyosin structure[5]), it would appear that their behaviour can be explained on the following assumptions : (1) that the tension developed during the active state is due to the formation of linkages in a sliding-filament actomyosin system[6], and that linkages are also made which involve a second system, characterized by the presence of filaments with paramyosin structure ; (2) that these latter linkages (to be called tonic linkages) break at a very slow rate and are responsible for the phenomenon of passive tension ; (3) that activation of inhibitory nerves increases the rate at which the tonic linkages break.

This explanation does not accept the 'catch mechanism' hypothesis, which holds that these muscles can maintain tension indefinitely without any expenditure of energy[7], because we find that in the absence of further activation tension decays to zero, and that a steady level of tension can only be maintained by periodic re-excitation of the muscle, that is, by a tetanic mechanism. The object of this communication is to summarize some of the physiological evidence in support of our hypothesis.

When the anterior byssus retractor muscle of *Mytilus* is stimulated with shocks several times threshold value, both excitatory and inhibitory nerves are activated and tension cannot be maintained for prolonged periods[4] (also Lowy, J., and Millman, B. M., unpublished results). Reduction of strength or frequency of stimulus gives a well-maintained tonic contraction (Fig. 1, *a* and *b*), and here inhibitory nerves are probably not activated. In this case the

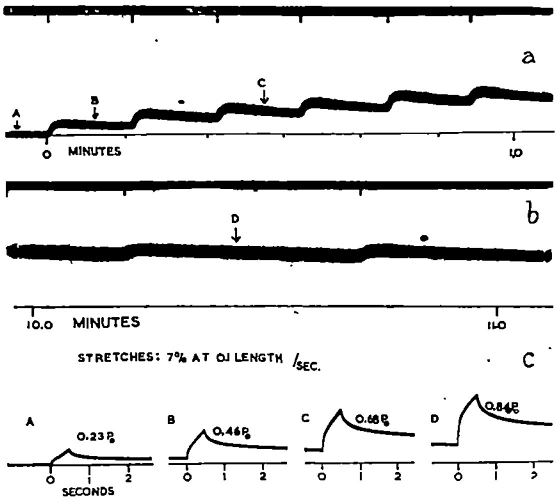

Fig. 1. (*a*) Anterior byssus retractor muscle of *Mytilus* stimulated directly by square wave pulses (15 V., 2 msec.) once every 10 sec. ; record of tension, increase upwards. (*b*) Same experiment ; after 4 min., frequency of stimulation had been reduced to one shock every 30 sec. ; a high level of tension (4 $kgm./cm.^2$) was maintained ; in this experiment stimulation was continued for 30 min. (*c*) In similar experiments the same muscle was stretched (within a range of muscle lengths where resting tension was negligible) at the points *A*, *B*, *C*, *D* indicated in *a* and *b* ; this revealed that resistance to stretch increased during the first 10 min. by a factor of about 4

resistance of the muscle to stretch increases with time (Fig. 1, *c*), suggesting (on our hypothesis) that the number of tonic linkages brought into action reaches a maximum only gradually.

Rapid stretch (at constant speed) of a muscle after the active state has decayed to zero, but at a time when some passive tension is still present, produces a large transient tension which takes several minutes to decay to zero. In the anterior byssus retractor muscle of *Mytilus*, the decay curve can be resolved into three exponential components with half-decay times of about 0·17, 2·2 and 45 sec. (Fig. 2). The time constants of the first two components are very close to those of the two exponential components in the stress relaxation curves of slow striated muscles[8]. As the filaments in striated muscle show no paramyosin structure, these two components are probably due to the actomyosin system. We have found the third component only in molluscan smooth muscles which have filaments with paramyosin structure and hold passive tension. The third component has a decay time of the same order of magnitude as isometric twitch tension, and is very likely due to the presence of tonic linkages. This idea is supported by the observations that after stimulation which also activates inhibitory nerves (or after treatment of the anterior byssus retractor muscle of *Mytilus* with 5-hydroxytryptamine which may act here as the inhibitory transmitter[9]), the third component is absent whereas the other two components remain unchanged; and that relaxation in an isometric twitch is accelerated whereas the time of rise of tension is not appreciably affected.

Further evidence for the presence of two systems comes from experiments in which the anterior byssus retractor muscle of *Mytilus* was stretched (at constant speed) during stimulation. If the stimulation also activates inhibitory nerves (and thus we assume diminishes the number of tonic linkages in existence at any instant) the form of the stretch curve resembles that given by tetanized frog sartorius muscle: a rapid increase in tension, followed by a more gradual rise (Fig. 3, *a* and *b*). It is conceivable that in both cases the fast phase is due to stretching of only the series elastic element, the linkages of the actomyosin system being extremely rigid. The point of inflexion of the curve could mark the stage at which these linkages break ('give'). The following slow phase might then represent the re-making and breaking of actomyosin linkages, and in the anterior byssus retractor muscle of *Mytilus* possibly also of some tonic linkages. During stimulation which does not activate inhibitory nerves, the tension produced during the slow phase of the stretch curve in the anterior byssus retractor muscle of *Mytilus* is appreciably greater (Fig. 3, *c*). This, and the differences in form of curves 3 *b* and 3 *c*, we consider to be due to the presence of tonic linkages.

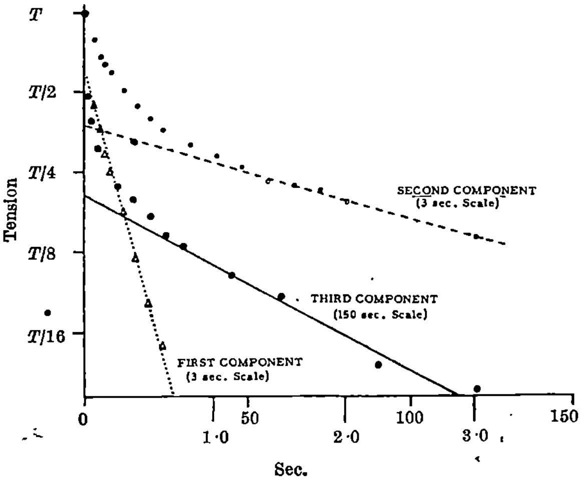

Fig. 2. Decay of tension produced by stretching the anterior byssus retractor muscle of *Mytilus* 10 per cent of its length at 0·24 length/sec., when a small amount of passive tension was present; the muscle was stretched within the range of lengths where resting tension was negligible. ●, Course of decay of tension; ○, decay of tension minus third component; △, decay of tension minus second and third components

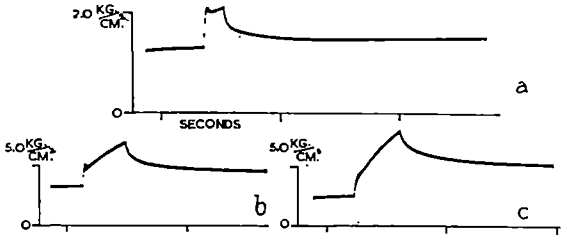

Fig. 3. (*a*) Sartorius of frog (0° C.) stretched 8 per cent of its length at 0·4 length/sec. during tetanic stimulation; isometric tension level, 1·3 kgm./cm.²; maximum tension above isometric produced during stretch, 0·8 kgm./cm.²; (*b*) anterior byssus retractor muscle of *Mytilus* (20° C.) stretched 10 per cent of its length at 0·24 length/sec. during stimulation that also activated inhibitory nerves; isometric tension-level: 3·5 kgm./cm.²; maximum tension above isometric produced during stretch: 3·8 kgm./cm.²; (*c*) same muscle and extent and speed of stretch as in (*b*); during stimulation that did not activate inhibitory nerves (12 volts direct current); isometric tension-level, 2·4 kgm./cm.²; maximum tension above isometric produced during stretch, 5·5 kgm./cm.²

Finally, the prolonged existence of these linkages is indicated by the observation that an anterior byssus retractor muscle of *Mytilus* stretched after stimulation (which does not activate inhibitory nerves) has ended, but at a time when some passive tension is still present, gives a stretch curve similar in form to that shown in Fig. 3 *c*. As might be expected, the amount of tension produced by such a stretch decreases with time after cessation of stimulation—as does passive tension.

Details of this work will be published elsewhere. The hypothesis put forward here owes much to discussions with Dr. Jean Hanson and is consistent with unpublished structural information obtained in this Laboratory by one of us (J. L.), Dr. Jean Hanson and Mr. G. F. Elliott.

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Quantitative Estimation of Amineoxidase

THE evidence linking brain function to amineoxidase activity[1] has stimulated a large production of papers[2]. The disagreements that have ensued[2] might well be a measure of the interest in these aminases. However, we attribute much of the discord to the accepted method of studying these trace enzymes, namely, respirometry. The present communication shows that respirometry is an erratic yardstick as compared with the measurements of ammonia (or primary amine) released by the amineoxidase reaction. The ease and accuracy of these latter micromethods have been shown previously[3-9].

For this study the currently popular monoamineoxidases were selected. In all probability, however, our conclusions apply to the entire group of enzymes concerned with oxidative deamination.

The reaction catalysed by monoamineoxidase has been written as follows[8]:

$$RCH_2NH_2 + H_2O + O_2 \rightarrow RCHO + H_2O_2 + NH_3$$

Therefore, in the presence of catalase, one molecule of oxidized substrate should release one molecule of ammonia and take up one atom of oxygen. That this is by no means always the case is shown by the two sets of 85 analyses summarized in Fig. 1. The two tests were performed concomitantly with a method presented previously[7]. Rat liver homogenate in various concentrations provided the enzyme and tyramine hydrochloric acid (100 μM) in potassium phosphate buffer (pH 7·4, μ0·1) completed the reaction mixture. The temperature was 37° C. and the atmosphere was oxygen. The broken line indicates the stoichiometric relationship between net oxygen uptake and net ammonia evolution. Almost all the data fell below the line, showing that more oxygen was taken up than can be attributed to the monoamineoxidase reaction alone. An excessive oxygen uptake was found also when salts of tryptamine, 5-hydroxytryptamine, epinephrine, norepinephrine, phenylethylamine, hydroxytyramine or benzylethylamine were used as substrates.

Several rat organs were tested in this fashion. The oxygen uptake was excessive to a variable degree. For example, in one experiment, liver and brain homogenates were compared. The O/NH$_3$ ratio for liver was 3·7 and for brain 1·9. Dark pigments were always formed when liver was tested, but these could not be discerned with brain.

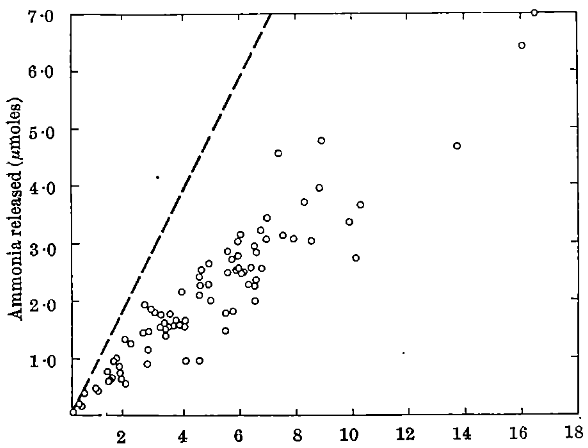

Fig. 1

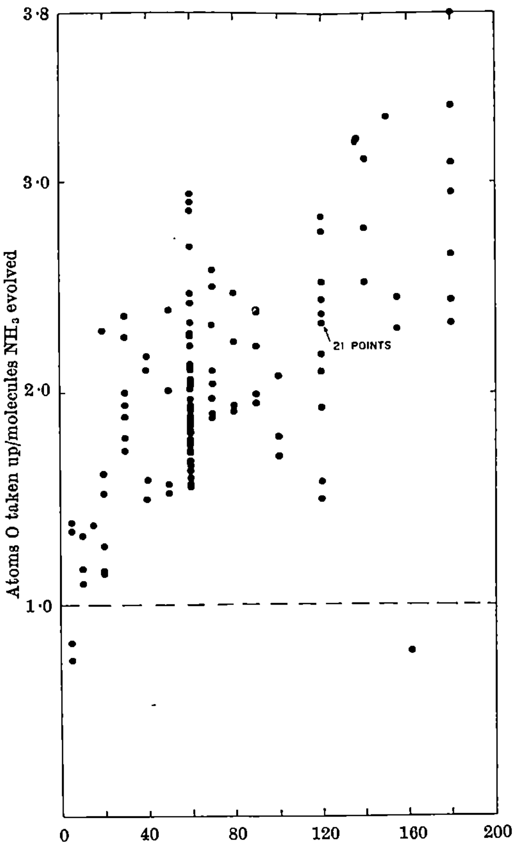

Fig. 2

Longer periods of incubation resulted in more pronounced oxidative excess. Fig. 2 shows that during the first few minutes of the reaction a surprisingly low oxygen uptake relative to the ammonia evolved may be observed. The broken line again indicates the stoichiometric relationship. Indeed, in experiments not illustrated here the O/NH$_3$ ratio was 0·3. (We had shown earlier[3] that no fixation of added ammonia can be detected under the conditions of these tests. In addition, whenever a limited amount of substrate was allowed to be completely deaminated, the recovery of ammonia was quantitative, while the oxygen uptake has varied.) Tentatively we have attributed this low O/NH$_3$ ratio to the lower sensitivity of the respirometer as compared with the ammonia measurement[3,5,7]. It has to be conceded, however, that these results might indicate the existence of an entirely separate deamination reaction which precedes oxidation. Also, the large spread of the data presented here suggests that the two processes might not be entirely linked. Regardless of the favoured explanation, it is evident from Fig. 2 that the uptake of oxygen became increasingly higher relative to evolution of ammonia with the advent of time.

Since secondary reactions contribute such a large proportion of the oxygen uptake, they may well determine the final score in studies of activation and inhibition of this enzyme. The discrepancies between two studies of intracellular localization[4,9] are probably due to differences in technique and suggest that respirometry might yield a distorted picture of this enzyme's partition in tissues.

An investigation was aimed at possibly eliminating the excess oxygen uptake. Several inhibitors were tested for their capacity to diminish specifically the oxygen uptake, but these experiments will be published separately. It is sufficient for the present argument to note that in experiments overlapping those of Creasey[10] there was essential agreement: precise addition of selected inhibitors may force the oxygen uptake almost to obey stoichiometry.

In conclusion, it seems obvious that the techniques for determining ammonia[3,5,7] would provide a more specific yardstick for the monoaminoxidase activity of tissues than does the popular respirometry. The latter may be coached to yield almost stoichiometric results, but the necessary chemical *tour de force* produces a complex and rigid system.

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A Rare Variant of B in a Human Blood Sample belonging to Group AB

During routine blood-group examination of healthy persons, one of the blood samples tested was found to exhibit unusual properties. The potent anti-A and anti-B test sera used agglutinated the erythrocytes quite well, whereas the serum of this AB blood (subgroup A_2B) reacted weakly at room temperature with B cells. The irregular agglutinin was no more active at 37° C. and reacted better at 4° C. (titre 8) than at 20° C. No auto-agglutination was observed. At 4° C. the serum agglutinated all of 15 B but neither 20 A nor 15 O cells samples simultaneously tested. The B specificity of this agglutinin was confirmed by absorption experiments with B erythrocytes and with purified blood group B substance. The B specificity of the agglutinogen in Mrs. Br.'s cells was ascertained by studying the action of several A and AB sera on them; the agglutinating action of A sera did not occur after absorption by normal B cells or purified B substance. The 'Br.' cells significantly absorbed the anti-B agglutinin in normal A sera, but less, however, than did A_2B cells used as control, and released it after elution more completely than did these A_2B cells. The 'Br.' cells were agglutinated by anti-H eel serum nearly as well as group O cells. The 'Br.' saliva inhibited the anti-A agglutinin at a high dilution, and the anti-B and anti-H agglutinins when more concentrated. Its inhibitory action on anti-H was not weaker than that of an A_2 control.

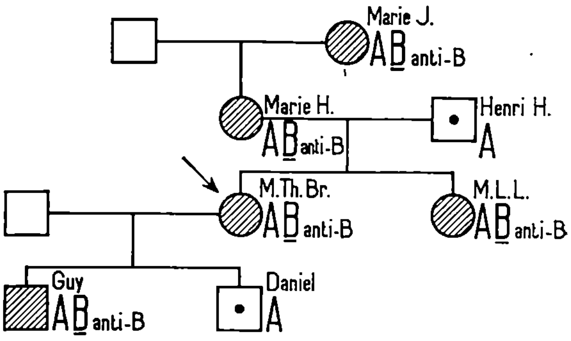

Fig. 1

This unusual subgroup was found in the blood of four other members of Mrs. Br.'s family. The four samples, belonging to the AB group, showed the same serological pattern as the 'Br.' blood. The irregular anti-B agglutinin was present in their serum, at a titre of 4 to 16 (at 4° C.). The four samples of saliva contained A, B and H substances but did not inhibit Mrs. Br.'s anti-B agglutinin.

The variant of B here described is quite different from the recently published cases of very weak B agglutinogens[1-4]. It would probably more likely resemble the case reported by Formaggio[5] (whose serum contained also an anti-B agglutinin) and perhaps those found in Pakistan by Boyd[6]. In considering its serological character, it appeared to us that it behaved in a way very similar to that of A_3 within the A group.

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Pressor Amines and Neuroblastoma

Isaacs, Medalie and Politzer[1] describe three cases of neuroblastoma in children in whom the 24-hr. excretion of noradrenaline in urine was 200–300 μgm. This is not a vast amount but may be abnormally high. The suggestion was that neuroblastoma is a tumour which, like phæochromocytoma, secretes pressor amines. On March 23, 1959, I obtained, by courtesy of Dr. P. T. Bray, a specimen of tumour infiltrating the left kidney, taken by Mr. H. Wade from a boy aged nine years at East Glamorgan Hospital, Church Village, Glamorgan, and kept frozen. This tumour was reported by the histopathologist to be typical neuroblastoma; the whole specimen weighed approximately 450 gm. of which some 300 gm. was tumour. 50 gm. was excised from the region which had been used for histology, cut up fine and homogenized with 50 ml. of water containing 5 mgm. ascorbic acid. This was spun at 3,000 r.p.m. for 15 min. and the supernatant examined on the blood pressure of the spinal rat injected with atropine and a ganglion blocker. Such a preparation responds to adrenaline 0·1 μgm., noradrenaline 0·05 μgm. or 5-hydroxytryptamine 3 μgm. with a pressor response.

The average of three assays indicated that the supernatant contained pressor activity equivalent to 0·25 μgm./ml. of noradrenaline. The supernatant also caused the smooth muscle of isolated guinea pig to contract smartly, in the presence of atropine sulphate 10^{-7} and mepyramine malleate 10^{-7}. This activity was reduced by lysergic acid diethylamide *pari passu* with that of added 5-hydroxytryptamine. The pressor action in the rat was also reduced but not abolished by *LSD*25. A dibenamine-like drug in a dose sufficient to abolish the pressor action of adrenaline, reduce that of noradrenaline but only in a dose sufficient to abolish the pressor action of adrenaline, reduce that of noradrenaline but only slightly affect that of 5-hydroxytryptamine reduced the effect of the extract.

The conclusion reached is : (*a*) this neuroblastoma contained pressor substances ; (*b*) these include noradrenaline and possibly adrenaline and 5-hydroxytryptamine ; (*c*) the amount is small compared with phæochromocytoma.

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Histochemical Changes in the Epiphyseal Cartilage during Rickets

In a previous communication[1], a method was described for staining the sites of the initiation of calcification in bone and teeth. This method consisted in treating the tissues with hot pyridine for 24 hr. prior to decalcification and then staining with sudan black. Sudan black stained the matrix around the hypertrophic cells in the epiphyseal cartilage just before these cells are removed by capillary erosion.

In order to test the hypothesis that the sudanophil material was concerned with calcification, rats with florid rickets have been examined. They were put on the Steenbock–Black diet[2] when they weighed 50–60 gm. ; 28 days later some were killed and others received one dose of 30 I.U. of vitamin D and were killed at daily intervals thereafter. The upper tibial epiphysis was examined by the method described above.

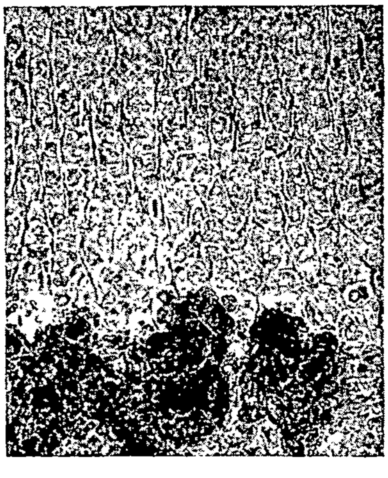

Fig. 1. Upper tibial epiphysis of rachitic rat, stained with sudan black after treatment with hot pyridine. No staining of the matrix between the hypertrophic cells is to be seen. (× *c.* 150)

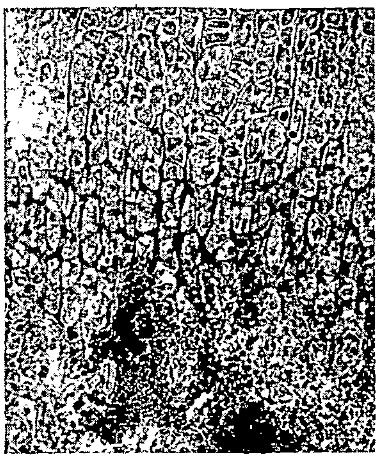

Fig. 2. Upper tibial epiphysis of rachitic rat, 7 days after dosage with 30 I.U. of vitamin D. Stained with sudan black after treatment with hot pyridine. Note re-appearance of sudanophil material in the matrix between the hypertrophic cells. (× *c.* 150)

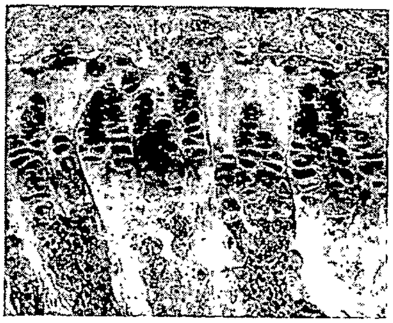

Fig. 3. Upper tibial epiphysis of old rat stained with sudan black after treatment with hot pyridine. The cartilage matrix does not stain, but the cartilage cells are filled with sudanophil granules. (× *c.* 150)

No sudanophil material was found in the epiphyseal cartilage of rats with untreated rickets (Fig. 1), but after dosage, the sudanophil material returned to the cartilage (Fig. 2) at the same time as calcification recommenced, as visualized by the von Kossa technique. In later stages, the material stained with silver extended deeper into the metaphysis as healing progressed ; but at all times sudan black stained only the matrix around the cells where calcification was starting.

These observations confirm the previous conclusion that the sudanophil material is intimately concerned with calcification. Experiments to be reported elsewhere have shown that under appropriate conditions the methylene blue extinction of the sudanophil material is lower than *p*H 2·6, indicating a highly acid mucopolysaccharide.

The upper epiphysis of the rat tibia does not close when growth stops, but is sealed off by a bony plate. The cartilage matrix no longer stains with sudan black, but the cartilage cells are full of sudanophil granules (Fig. 3). The same is often seen in the hypertrophic cells of rachitic cartilage, and possibly the cells store this substance when calcification does not or cannot take place.

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Electrophoretic Patterns of the Serum Proteins of Sheep infected with *Hæmonchus contortus*

The subcutaneous injection of living *H. contortus* into worm-free sheep appeared to provide partial protection against subsequent challenge[1]. Changes in the electrophoretic pattern of the serum proteins might be expected[2–6], and the appearance of the pattern has been followed.

Sera from sheep, untreated control (3), injected with dead larvæ (3), and injected with live larvæ (3) were collected prior to injection, after two injections and subsequent to challenge. No change in the electrophoretic pattern by filter paper electrophoresis was apparent. In a more detailed quantitative study by column electrophoresis[7] two of the animals infected with live larvæ showed a slight (1 per cent) increase in β-globulin. No increase in γ_1- or γ_2-globulin was observed.

The experiment was repeated with a further six sheep all of which became refractory to re-infection as a result of successive injections followed by challenge doses. The electrophoretic patterns of the serum proteins from three animals showed a pronounced intensification of the β-globulin. There was a less-marked change in one animal; and the pattern in the two others remained unchanged.

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Pharmacology of a Tranquillizing Principle in *Paspalum scrobiculatum* Grain

Paspalum scrobiculatum Linn. (Fam. Gramineae; name in Marathi language, *harik*) is cultivated in various parts of India for the grain, which forms the staple diet of the poor rural population. One variety of this plant yields a toxic crop after a favourable rainfall. The toxin is believed to reside in the husk of the grain. The grain of such a crop is detoxified before use by a special process.

The grain was kept in ethanol at room temperature for 1–2 days. The ethanol extract was evaporated to dryness by heating on a water-bath. The dry residue was thoroughly mixed with dilute hydrochloric acid. The dilute acid was then separated from the undissolved portion and dried by heating on a water-bath. The residue or active fraction was dissolved in distilled water before use.

The original active substance is soluble in boiling water, acidified water, ethanol, chloroform and ether. It can be partly extracted from alkaline aqueous phase by ether. Thus it behaves like an alkaloid. It is biologically active after keeping in strongly acidic or alkaline media even at 100° C. Aqueous solution of the active fraction (which appears crystalline under the microscope) gives green fluorescence in ultraviolet light. Two samples of grain gave yields of 0·025 and 0·066 per cent of the active fraction respectively. The active fraction does not give the colour reaction suggested by Sundaram Ayyar and Narayanaswamy[3]. (In their animal experiments those authors observed only tremors and death.)

Various samples of grain (comprising from 1 to 50 gm.) and the various fractions of extraction were added to the diet of 11 dogs in 53 experiments. The active fraction, prepared from samples of 1–50 gm. of grain, was also administered by intravenous or intraperitoneal injection into 6 dogs in 33 experiments.

Oral administration produces tranquillity and lack of interest in the environment. The dogs sit quietly, crossing the forelimbs and looking vacantly into space. Hostile dogs become much less aggressive. Larger doses cause tremors, rigidity of face, trunk and limbs not unlike human Parkinsonism. There was no miosis of the eye in these animals. The effects usually persist for 6–8 hr.

In 5 dogs and 2 cats, after anæsthesia, intravenous injection of the active fraction did not produce any relevant change in blood pressure and respiration, except depression of the carotid sinus reflex in 2 dogs and 1 cat.

In 10 rabbits, 11 guinea pigs, 4 cats and 21 albino rats, the active fraction produced definite tranquillity. In rabbits larger quantities produce clonic convulsions and death.

The effect of the active fraction on hexobarbitone sleeping time was studied in mice, following the technique of Brodie *et al.*[1]. The hexobarbitone sleeping period was significantly (*t*-test, $P < 0{\cdot}01$) prolonged in mice after injection of the active fraction (Table 1).

Like reserpine and chlorpromazine, the active fraction produces tranquillity and symptoms of 'Parkinsonism' in dogs. Unlike chlorpromazine, reserpine produces parasympathomimetic effects and release of 5-hydroxytryptamine from the central nervous system. The active fraction does not produce clear-cut parasympathomimetic effects (such as

Table 1. HEXOBARBITONE SLEEPING PERIOD IN MICE
Hexobarbitone, 100 mgm./kgm. intraperitoneally. Active fraction given ½ hr. before hexobarbitone

Drug	Source of active fraction	Sleeping time (min. ± *S.D.*)	No. of mice used
Control (hexobarbitone)		23 ± 6·5	17
Active fraction + hexobarbitone	6 gm. grain	47 ± 23·4	6
	12 gm. grain	101 ± 38·0	14
	24 gm. grain	123 ± 12·9	7
Active fraction + hexobarbitone		53 ± 8·3	12
Active fraction + hexobarbitone 2 days later		50 ± 11·3	11

Table 2. HEXOBARBITONE SLEEPING PERIOD IN MICE

Reserpine (5 mgm./kgm.) administered 1 hr. before hexobarbitone (100 mgm./kgm.) administered intraperitoneally. Only hexobarbitone given next day to assess the residual effect of reserpine. Chlorpromazine 2·5 mgm./kgm.

Drug	Sleeping time (min. ± *S.D.*)	No. of mice used
Control (hexobarbitone)	19 ± 7·3	32
Reserpine + hexobarbitone	60 ± 14·0	21
Hexobarbitone, 1 day later	17 ± 6·7	32
Reserpine + hexobarbitone, 2 days after first injection	17 ± 6·0	22
Chlorpromazine + hexobarbitone	45 ± 7·2	13
Chlorpromazine + hexobarbitone, after 2 days	44 ± 11·8	12

miosis). A much simpler experiment is therefore to test whether it releases 5-hydroxytryptamine from the central nervous system. Mice received intraperitoneally chlorpromazine or reserpine or the active fraction, followed by hexobarbitone, and their sleeping time was noted. Two days later the same mice received the same substance, and hexobarbitone and the effect on sleeping time was again noted.

The active fraction and chlorpromazine when re-administered after 2 days were still active in prolonging the hexobarbitone sleeping time, whereas reserpine, which depletes the central nervous system of 5-hydroxytryptamine for about 5 days (Shore *et al.*[2]), was inactive in prolonging sleeping period in mice after 2 days (Table 2).

Further work is in progress.

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Spore Germination in *Agaricus campestris* L. ex Fr.

THE presence of growing mycelium of *Agaricus campestris* in medium containing spores of this fungus has been shown to stimulate germination[1,2]; but there are no reports of a detailed analysis of the effect.

Recent experiments here have shown that a volatile metabolite secreted by the mycelium is a stimulating factor. This was first demonstrated by showing that spores held on a nutrient medium in the air above actively growing cultures of the fungus, or above medium taken from such cultures, germinated better than those held above uninoculated control medium.

The presence of a volatile metabolite was confirmed by drying gases from cultures with phosphorus pentoxide, and passing them through a container cooled in liquid air. A crystalline product was obtained which was a volatile liquid at room temperature. The germination of spores on nutrient media was strongly stimulated by the presence of an aqueous solution of this material in the same container, but not in contact with them.

Analysis of this material by means of a mass spectrometer has shown the presence of an olefin which is probably 2 : 3-dimethyl-1-pentene. No other compound has been detected during this analysis. It has not yet been possible to obtain synthetic material for testing, but it appears likely that this substance is the stimulating factor.

These observations seem of interest in relation to the many reports[3] of the production of unsaturated hydrocarbons by plant organs. In many of these cases the gas has been identified as ethylene, but the tests used have not usually been sufficiently rigorous to exclude the presence of other olefins[4]. Trimethylethylene has been reported as a self-inhibitor of germination of spores of *Puccinia graminis* var. *tritici*[5]. These observations may also relate to the reports of a volatile substance which inhibits strand formation and fruit-body formation if it is allowed to accumulate in mushroom beds[6–8].

The work is continuing and a detailed report will be published elsewhere.

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BIOCHEMISTRY

α-Helices and a New Polypeptide Fold in Poly-β-Benzyl-L-Aspartate

IN Moffitt's expression for the variation of the optical rotation of an L-polypeptide in the α-helical form with wave-length[1,2], the constant b_0 has been found to have values between −400 and −700 deg. cm.^{2}/decimole; the negative value is certainly associated with a right-handed screw sense in poly-L-alanine[3]. Recently, values up to 631° have been reported for poly-β-benzyl-L-aspartate ($[CO.NH.CHCH_2CO.OCH_2C_6H_5]_n$) in chloroform solution by Blout and Karlson[4]. This positive value of b_0 may indicate either the 'structural' anomaly of a left-handed screw sense, or alternatively an 'optical' anomaly due to interaction between peptide and side-chain chromophores or consequent upon some minor structural peculiarity. We have confirmed the anomalous result and have examined the polymer by a variety of techniques.

Direct evidence as to the configuration of the polymers exists only for the solid state. Films cast from chloroform solution and oriented by stroking give an X-ray diffraction pattern which is undoubtedly that of the α-helix, with a meridian reflexion at 1·5 A.

We have measured the residue rotation and calculated b_0 (assuming λ_0 to be 2120 A., as in poly-γ-

Table 1. PROPERTIES OF POLY-β-BENZYL-L-ASPARTATE

Preparation	Solvent	η_{sp}/c*	b_0†	$[R_{\text{vac.}}]_{5461}$†
417*B*	Dichloracetic acid	0·110	−257°	−26·8°
412*A*		0·190	−282	−29·4
429*A*		0·458	−260	−28·1
429*B*		0·544	−250	−28·5
417*B*	*m*-Cresol		−70	−58
412*A*			+327	−129
429*A*			+526	−151
429*B*			+534	−150
417*B*	Chloroform		+450	−215
412*A*			+566	−250
429*A*			+660	−268
429*B*			+665	−274
417*B*	Film cast from chloroform		−3,560	+290

* c = 0·5 gm./100 c.c.

† Optical rotations measured at 20° C.; concentrations 0·5 per cent w/v or less.

benzyl-L-glutamate) for a number of preparations of poly-β-benzyl-L-aspartate of different molecular weights, in solvents of different polarity. A representative selection of these results is given in Table 1, together with viscosities measured in dichloracetic acid, which give a measure of molecular weight. In dichloracetic acid the values of b_0 and $[R_{\text{vac.}}]$ are not correlated with molecular weight. In *m*-cresol these quantities change greatly in magnitude and also in sign, and in chloroform a less dramatic but still significant change may be seen. In both these solvents a limiting value has been approached in the two specimens of highest molecular weight. We take this to mean that in dichloracetic acid the polymer is in a random, solvated coil in spite of the high value of b_0. In chloroform and to a lesser extent in the more polar *m*-cresol, a fraction of the polymer must be in a helix, the specimens of higher molecular weight being almost entirely in this form. This is reasonable, but the values of b_0 are unlike those in poly-γ-benzyl-L-glutamate ($[CO.NH.CHCH_2CH_2CO.OCH_2C_6H_5]_n$) in three respects. As mentioned above, b_0 is positive in the helix form. Secondly, it differs considerably from zero in the random coil form and finally it changes sign and becomes numerically very much greater in films cast from a non-polar solvent. Films of poly-γ-benzyl-L-glutamate are found to have a value of b_0 of approximately the same magnitude (and negative sign) as solutions containing α-helices of that polymer. It is evident that some kind of optical anomaly is present in the aspartate polymer, but nevertheless the positive value of b_0 may mean that the helix has a left-hand screw sense.

We have measured the rate of replacement of NH by ND in a solution of poly-β-benzyl-L-aspartate in methylene chloride containing 1 per cent (v/v) of O-deuterated acetic acid. The rate is many times greater than that for poly-γ-benzyl-L-glutamate (of a similar reduced viscosity in dichloracetic acid) under similar conditions, leading to the conclusion that the helical configuration of the aspartate polymer is less stable than that of the glutamate.

Further evidence of this comparative instability is provided by the behaviour of solid films on heat treatment. Oriented films of the α-form of poly-γ-benzyl-L-glutamate are stable to heating *in vacuo* at about 170° C. for some hours, becoming more crystalline[5]. Similar treatment of the aspartate polymer, however, produces a specimen in which the X-ray diffraction pattern is replaced by a completely new one. This new form (which we propose to call the ω-form) has a tetragonal (not hexagonal) unit-cell base, and a meridian reflexion at 1·3 A., but none at 1·5 A. The five layer lines observed correspond at least approximately to orders of a strong layer line at 5·2 A. The infra-red dichroism of the peptide bands is not appreciably altered by the heat treatment, so that the new form is probably produced with little change in the atomic positions within one residue. A fold described by Bragg, Kendrew and Perutz[6] as 4_{13}, topologically similar to the α-helix (being formed by the same 13-membered hydrogen-bonded rings) but with amide groups not quite planar, may be found to fit the new X-ray pattern. This fold has a residue repeat of about 1·3 A., and having a four-fold screw axis would be expected to pack tetragonally. The measured density of the heated polymer is 1·31 gm./c.c., in satisfactory agreement with the crystallographic density 1·36 for a tetragonal unit cell with $a_0 = b_0 = 13 \cdot 85$, $c_0 = 5 \cdot 2$ A. containing four residues.

The reason for the instability of the α-helix in the aspartate polymer is probably connected with interaction between the peptide groups and the side-chains. In the new form the ester C=O band is at 1,727 cm.$^{-1}$, while in the α-helix form it has the usual frequency 1,737 cm.$^{-1}$; it has also acquired appreciable parallel dichroism. The peptide C=O band, on the other hand, is at 1,664 cm.$^{-1}$ and 1,675 cm.$^{-1}$ in the α-helix and new forms, respectively. These peptide C=O frequencies are higher than any so far reported for polypeptides made from a single optical isomer. When the heat-treated polymer is dissolved in chloroform, it is found that films cast from the solution have infra-red spectra identical with those of the unheated films.

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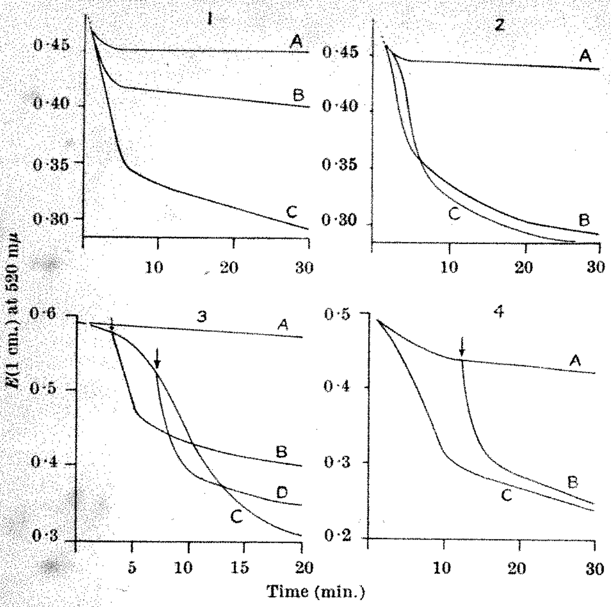
Effects of 2 : 4-Dinitrophenol and Other Agents on the Swelling of Isolated Mitochondria

WE have offered evidence[1] that, under various conditions, the swelling of isolated rat-liver mitochondria is dependent on the presence of oxidizable subtrates. For example, if the particles are stored for one day in 0·44 *M* sucrose at 0° C. ('aged'), phosphate or thyroxine no longer causes them to swell unless certain oxidizable subtrates, for example, β-hydroxybutyrate, are added as well. Reasons were given for supposing that, in many circumstances, swelling is dependent on mitochondrial respiration. We suggested that, in view of the stabilizing action of 0·1 m*M* 2 : 4-dinitrophenol[2], any effect of respiration on swelling may be exerted through coupled phosphorylation (see also ref. 3); however, after a more extensive



Figs. 1–4. Swelling of mitochondria at 20° C. All cells contained 10 m*M* phosphate, 25 m*M* *tris* chloride buffer *p*H 7·5 and 0·3 *M* sucrose. Fig. 1. 2 : 4-Dinitrophenol added initially; fresh mitochondria. Curve *A*, 0·1 m*M* dinitrophenol; curve *B*, 0·02 m*M* dinitrophenol; curve *C*, control. Fig. 2. As for Fig. 1, but with 2 m*M* DL-β-hydroxybutyrate. Fig. 3. 0·1 m*M* dinitrophenol added (arrows) during swelling in the presence of 1 m*M* D-β-hydroxybutyrate; aged mitochondria. Curves when dinitrophenol added (*A*) at zero time; (*B*) at 3 min.; (*D*) at 7 min.; (*C*) control. Fig. 4. Inhibition with oligomycin (0·4 μgm./ml.) and release (arrow) by 0·01 m*M* dinitrophenol; 2 m*M* DL-β-hydroxybutyrate present; fresh mitochondria. Curve *A*, oligomycin; curve *B*, oligomycin followed by dinitrophenol; curve *C*, control

study of the effects of uncoupling agents we think that this is unlikely to be so. Thus, lower concentrations of 2 : 4-dinitrophenol, and dicoumarol, will, under some conditions, accelerate the swelling induced by phosphate, and even 0·1 m*M* dinitrophenol will increase the rate of swelling if it is added after the mitochondria have been previously incubated in the presence of phosphate.

Twice-washed mitochondria were prepared and studied under our routine conditions[1]. With fresh mitochondria, in the absence of added substrate, 0·1 and 0·02 m*M* dinitrophenol, present initially, inhibited swelling induced by 10 m*M* phosphate with a lag period of 2–4 min. (Fig. 1). Here the lower concentration of dinitrophenol was scarcely less effective than the higher, but in the presence of 2 m*M* DL-β-hydroxybutyrate and phosphate (Fig. 2) 0·02 m*M* dinitrophenol slightly accelerated the swelling, whereas 0·1 m*M* was still strongly inhibitory. With aged mitochondria under the same conditions, 0·02 m*M* dinitrophenol slowed the swelling considerably. However, after they had been pre-incubated with β-hydroxybutyrate for 8 min. at 20° C., subsequent addition of phosphate together with 0·02 m*M* dinitrophenol produced a swelling response similar to that obtained with fresh mitochondria, that is, swelling with phosphate and dinitrophenol was more rapid than that with phosphate alone. Consistent with this finding, addition of even 0·1 m*M* dinitrophenol to fresh or aged particles in the process of swelling induced by phosphate with β-hydroxybutyrate caused acceleration (Fig. 3).

With fresh mitochondria, when phosphate was replaced by thyroxine (7 μ*M*), 0·1 m*M* dinitrophenol completely arrested swelling when present from the start, but when it was added later swelling was accelerated. This occurred in the presence of β-hydroxybutyrate, with fresh and aged particles. Dicoumarol (5–10 μ*M*) behaved similarly to dinitrophenol in this respect. With fresh particles 10 μ*M* dicoumarol had an effect on phosphate-induced swelling similar to that of 0·02 m*M* dinitrophenol (Fig. 2), except that the initial fall was more rapid and the extent of swelling less. With aged mitochondria, in the presence of β-hydroxybutyrate, swelling induced by phosphate was completely stopped by dicoumarol added initially; later addition of dicoumarol caused acceleration, as was the case with dinitrophenol.

These acceleratory effects of dinitrophenol and dicoumarol could not be reproduced by delayed additions of other known inhibitors[4] of swelling, namely, manganese chloride, ethylenediamine tetraacetate, cyanide or adenosine diphosphate, or by low concentrations of antimycin *A* or amytal[1,5]. Among other uncouplers tested, mepacrine[6] (1 m*M*) was relatively ineffective in preventing the phosphate-induced swelling of fresh mitochondria, but was strongly inhibitory with aged particles; lower concentrations down to 0·05 m*M* failed to produce acceleration. In contrast to mepacrine, aureomycin (0·07 m*M*) completely stopped the swelling of fresh mitochondria—indeed, the optical density rose above its initial value—but was only partially effective with aged mitochondria.

Oligomycin inhibits respiration, and this inhibition is reversed by dinitrophenol, which suggests that this antibiotic acts on the phosphorylation system rather than on the respiratory chain[7]. With fresh mitochondria in the presence of β-hydroxybutyrate, oligomycin (0·4 μgm./ml.) strongly inhibited the swelling produced by phosphate; 0·01 m*M* dinitrophenol (Fig. 4), or 3 μ*M* dicoumarol, abolished this effect. With aged particles oligomycin no longer inhibited swelling. It also failed to affect swelling induced by thyroxine, even with fresh mitochondria.

The acceleratory effects of dinitrophenol and dicoumarol, and particularly the reversal by dinitrophenol of the inhibition of swelling by oligomycin, indicate that swelling may occur when phosphorylation is uncoupled, and suggest that the effect of respiration on swelling is not exerted through the phosphorylation process. The inhibition of swelling by high concentrations of dinitrophenol and other uncoupling agents might be due to actions on the mitochondrial structure or to a deleterious effect on co-factors of respiration. It may be noted that aureomycin in low concentrations inhibits respiration as well as phosphorylation[8].

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Spectrophotometric Investigation on the Orcein Derivative of Elastin

IRREVERSIBILITY of the reaction between orcein and elastin[1] and the strength of the bond, which varies with different dyestuffs and proteins, supports the hypothesis of purely chemical bond rather than that of a hydrogen bond or an adsorption complex.

The existence of a chemical bond may be demonstrated spectrophotometrically, employing the principle of conjugation bathochromy: it is known that conjugation of two chromophore groups produces a shift of the absorption maximum towards longer wavelengths.

Orcein and its reaction product with elastin (orceinelastin) have been spectrophotometrically investigated. Orcein was dissolved in a *p*H 8·9 buffer. Purified orceinelastin, obtained by complete removal of the free colour from the reacted elastin, was brought into solution by digestion with elastase (the elastolytic enzyme of Balò and Banga) at *p*H 8·9.

The absorption spectrum of the coloured digestion products of orceinelastin was found to be the same as orcein except for a bathochromic shift of the absorption maximum from 574 to 589 mμ. Since a bathochromic shift is a property of the conjugation link only, the existence of a sharing bond between orcein and elastin is indicated.

By comparing extinction values of pure orcein with digested orceinelastin ones, the stoichiometry of the compound was found to be 1·265 gm. ($2 \cdot 53 \times 10^3$ moles) orcein/100 gm. elastin. This quantity was found not to depend, within large limits, on the reaction temperature and orcein concentration. This provides further evidence that there is a chemical bond in orceinelastin. The only value reported in the literature is by Weiss[2] (no methods specified) of 2×10^2 moles/100 gm. elastin.

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Ultra-violet Fluorescence of Quinine Sulphate for Detection of Phosphate Ester Spots on Paper

A WIDE variety of phosphate esters have great importance as intermediates in biological reactions. Development of adequate procedures for the chromatography and detection of these phosphate esters has, in many respects, lagged behind. With the exception of the method of Runeckles and Krotkov[1], which was developed as a modification of the procedure of Wade and Morgan[2], the detection of phosphate esters on paper chromatograms has been very laborious and relatively insensitive. Most of the molybdate procedures, in addition to requiring many manipulations, have the disadvantage of employing perchloric acid, which weakens the paper and causes some charring during heating.

This communication reports a simple dip procedure by which phosphate spots containing as little as 0·007 μmole of phosphorus can be detected. The phosphate spots are located by immersing the developed and dried paper in a solution of 0·5 per cent quinine sulphate·$2H_2O$ in absolute ethanol. After drying the paper at room temperature for a few minutes, the phosphate spots can be detected by examining the paper under ultra-violet light in a darkened room. The spots show up as light areas against an intense grey-blue fluorescent background.

The best results were obtained with a low-pressure mercury source filtered to exclude visible light and producing predominantly ultra-violet radiation in the 2537-A. region. A long-wave lamp with ultra-violet radiation in the 3600-A. region and also filtered to exclude visible light was, in general, found to be only a little less satisfactory than the 2537-A. source.

In only one case was a qualitative difference noted between the two ultra-violet sources; that was with adenosine triphosphate, guanosine triphosphate and uridine triphosphate on a paper developed with a butanol, acetic acid and water solvent. With the 3600 A. source all three compounds appeared as light spots against a fluorescent background, but with the 2537 A. source, the first two appeared as dark blue spots while the uridine triphosphate appeared as a light spot against the fluorescent background.

The quinine sulphate dip, in addition to its ease of use, offers the great advantage of employing an alcohol-soluble and apparently non-reacting spot-detecting compound. After marking the spots under ultra-violet light as rapidly as possible, one can wash the bulk of the quinine sulphate off the paper with absolute ethanol, thus leaving the phosphate ester spots unmoved and free for elution and further determinations. The spots may also be left on the paper, following the alcohol wash, for study by other spot-detection procedures such as specific ketose reactions.

The sensitivity of this dip procedure for detecting various phosphate compounds which were developed on paper chromatograms is shown in Table 1.

Table 1. DETECTION OF COMPOUNDS CONTAINING PHOSPHORUS WITH QUININE SULPHATE ON DEVELOPED PAPER CHROMATOGRAMS

Substance tested	Smallest amount of test material showing a strong spot (μgm. free acid)
Orthophosphate	0·7
Pyrophosphate	0·7
Phosphoglyceric acid	3
Dihydroxyacetone phosphate	3
β-Glycerophosphoric acid	3
Fructose-6-phosphate	4
Fructose-1,6-diphosphate	3
Galactose-1-phosphate	4
Glucose-1-phosphate	4
Uridine monophosphate	2
Uridine diphosphate	1
Uridine diphosphoglucose	2
Uridine triphosphate	1
Adenosine triphosphate	2
Guanosine triphosphate	2

Quinine sulphate is not selective for phosphate esters, but other organic compounds which might be present in chromatograms of this type, such as free sugars and amino-acids, must be present in relatively high concentrations before they are detected under ultra-violet light. Free sugars are not detected in amounts smaller than 40 μgm. per spot and only a few of the amino-acids tested could be detected in amounts as small as 15 μgm. per spot. A confirmatory ninhydrin dip or spray to detect any amino-acids which might be present can be run on the same paper following the quinine sulphate dip and subsequent ultra-violet examination. The quinine sulphate left on the paper does not interfere with the ninhydrin test. Purines, pyrimidines and nucleosides show up strongly. This was expected, since fluorescent procedures such as that of Pfennig[3] have been used to enhance the natural quenching of these compounds under ultra-violet light.

The paper ionophoresis and chromatography techniques of Runeckles and Krotkov[1] are ideally suited for this dip procedure since volatile buffers and solvents are used. The presence of inorganic salts in the developing solvents for the papers causes rather severe interference with spot detection. Interference from compounds such as trichloracetic acid, however, can be minimized by washing the papers with absolute ethanol or other suitable solvents prior to the quinine sulphate dip.

The dip procedure has worked well with a variety of papers including Whatman No. 1 and Schleicher and Schuell No. 507. In most cases, prior washing of the paper has been found beneficial. With some papers, however, washing has not always been necessary if the solvent front is sufficiently removed from the spots under study.

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Isolation of Kojibiose from Honey

Previously, we reported[1] that fifteen honey samples produced mainly in the Tohoku region of Japan were analysed, and sugar components of one kind of honey (*Lespedeza bicolor*) were fractionated by chromatography, using a carbon : 'Celite' column, and the sugars in each fraction were estimated. Glucose, fructose, sucrose, maltose, melezitose, eight di- or tri-saccharides and nine higher oligosaccharides were detected by paper chromatography, and fifteen spots of them contained ketose.

On the other hand, it has been reported that Goldschmidt *et al.*[2] detected *iso*maltose in honey by paper chromatography and White *et al.*[3] isolated nigerose from honey.

We now report the isolation of kojibiose. Honey (*Lespedeza bicolor*, 300 gm.) was fractionated with a carbon : 'Celite' column (550 mm. × 125 mm.) using water (22 l.), and ethanol, 2·5 per cent (22 l.), 5 per cent (14 l.), 10 per cent (18 l.), 15 per cent (18 l.), 20 per cent (14 l.), 25 per cent (12 l.) and 30 per cent (30 l.) as successive elution solvents. Kojibiose was detected in 2·5–5 per cent ethanol effluent by paper chromatography. The effluent portions containing kojibiose from three columns (900 gm. honey) were combined (16·5 gm. sugar mixture). These portions were contaminated with a considerable amount of *iso*maltose, two oligosaccharides containing ketose, glucose, fructose, sucrose and a trace of leucrose.

The sugar mixture was then rechromatographed on a carbon : 'Celite' column (530 mm. × 80 mm.) using the gradient elution method with 0–3·0 per cent aqueous ethanol containing borate buffer (*p*H 10·0)[4]. Substantially perfect separation of kojibiose from other sugars was achieved. The water fractions contained monosaccharides, and the 0·5–1·5 per cent ethanol fractions contained *iso*maltose and several sugars containing ketose. Kojibiose appeared in the 2·0–3·0 per cent ethanol fractions.

By the removal of borate from the sugar complex by repeated distillation with methanol, 1·3 gm. of chromatographically pure kojibiose was obtained. Since direct crystallization of the sugar acetylated in the usual way was not successful, the benzene solution of the crude acetate was poured on a column (300 mm. × 40 mm.) of 'Magnesol' : 'Celite' (5 : 1) and developed with 1,000 ml. of benzene/*t*-butanol (100 : 1 by vol.). A zone appeared at 165–215 mm. from the top of the column, which, by means of potassium permanganate streak indicator, was sectioned from the column and eluted with acetone. Removal of the solvent left 0·5 gm. of syrup, from which 208 mgm. of fine prisms were obtained upon crystallization from ethanol. It had m.p. 117–118° C., $[\alpha]_D$ + 113·8° (*c.* 1·2 in chloroform).

The upper portion (10–165 mm.) of the column was eluted with acetone, and removal of the solvent left 0·7 gm. of syrup. This syrup was rechromatographed on the 'Magnesol' : 'Celite' column. From the zone at the bottom of the column, 0·1 gm. of syrup was obtained which upon crystallization from ethanol gave 11 mgm. of fine prisms. It had an m.p. of 166° C.

Neither acetate showed depression of melting point on admixture with α- and β-kojibiose octa-acetates (166° and 117° C.) synthesized chemically by Matsuda[5].

We wish to acknowledge our indebtedness to Mr. K. Matsuda for his advice.

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Purification of Bacterial Neuraminidase (Receptor-destroying Enzyme)

Neuraminidase is the name now given to an enzyme the action of which is the hydrolytic cleavage of the glycosidic bond joining the keto group of N-acetylneuraminic acid to D-galactose or D-galactosamine[1]. The enzyme was discovered in 1946 when Burnet, McCrea and Stone[2] found that filtrates of *V. cholerae* rendered human cells inagglutinable by influenza viruses. The factor responsible for this action was called the receptor-destroying enzyme by Burnet and Stone, who obtained some purification of the enzyme present in *V. cholerae* (strain 4 *Z*) filtrates by adsorption to and elution from red cells[3]. This technique was later incorporated into a three-step procedure for the partial purification of the enzyme[4]. Crude or semi-purified receptor-destroying enzyme has since been used as a standard reagent in influenza virus studies: further work in this field, together with increasing interest in the biological and chemical properties of compounds containing

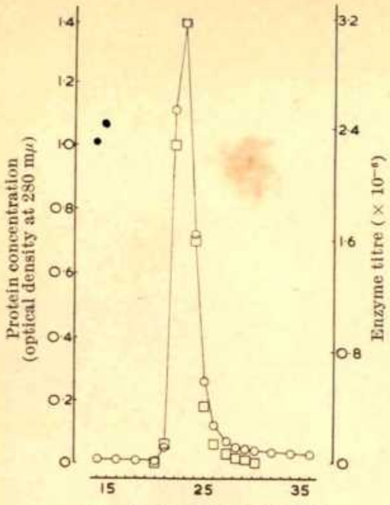

Fig. 1. Purification of neuraminidase by chromatography on hydroxyapatite. Elution pattern using a concentration gradient of phosphate buffer, pH 6·8. ○—○, Protein concentration; □—□, enzyme titre

N-acetylneuraminic acid, have emphasized the need for the pure enzyme.

Improved yields of enzyme have recently been obtained using a medium composed of bovine colostrum dialysate to which were added peptone and glycerol[5]. Following the growth of *V. cholerae* in such medium and subsequent heating to kill the organisms, filtration yields a crude extract from which it has now been possible to purify and crystallize the enzyme.

Enzyme estimations were carried out by the biological method previously described[6]. Protein concentrations were assessed by tyrosine estimations[7], by absorption at 280 mμ or by refractometry.

The purification process is briefly as follows.

(1) Cold methanol is added to 36 litres of crude extract (pH 5) to give a final concentration of 60 per cent. The precipitate which forms is suspended in and dialysed against water and a clear extract is obtained by centrifugation.

(2) Neuraminidase in the extract (sodium chloride, 0·8 per cent; calcium chloride, 0·1 per cent; pH 8·5, 2° C.) is adsorbed on to fresh, washed, packed human red cells and eluted from the cells in the presence of ethylenediamine tetraacetate (0·01 M, pH 7, 20° C.).

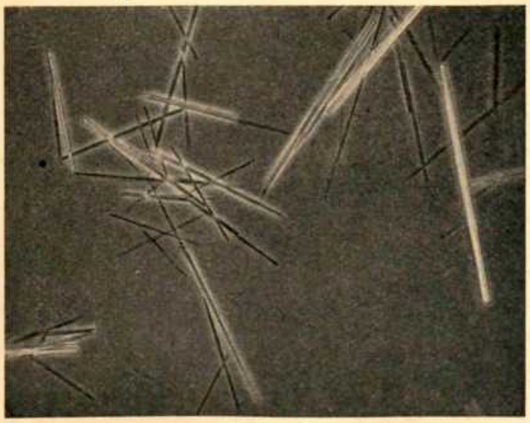

Fig. 2. Crystalline neuraminidase (phase contrast, × 300). Photograph by Mr. E. Matthaei

(3) An equal volume of saturated ammonium sulphate solution (pH 7, 2° C.) is added to the clarified eluate (2° C.). The precipitate which forms is dissolved in and dialysed against buffered saline (0·1 M sodium chloride, 0·001 M phosphate, pH 6·8).

(4) The enzyme is adsorbed on to a column of hydroxylapatite[8] and the column developed with a gradient of phosphate-buffered saline, pH 6·8 (phosphate concentration 0·001–0·25 M), the eluate being collected in a fraction collector. The enzyme elutes as a single peak, which, on re-chromatography, yields typically a result like that shown in Fig. 1. In the experiment shown, tubes 22, 23 and 24 were pooled and dialysed against water.

(5) The dialysed solution is concentrated to about 2 ml., adjusted to about pH 4·3 and then gently shaken at 2° C. for 2–3 days, when crystals appeared (Fig. 2).

The crystalline enzyme has an enzymic activity of about $8 \cdot 6 \times 10^6$ units/mgm. of protein (protein estimated by refractometry). This represents a purification of approximately 1,000-fold. In three experiments the overall yield of crystalline enzyme was 33, 30 and 52 per cent.

Details of the purification process and properties of the enzyme will be published elsewhere.

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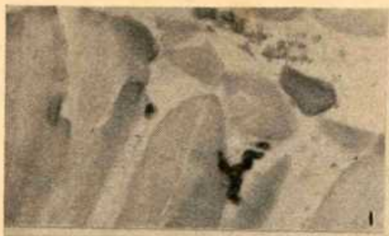
PATHOLOGY

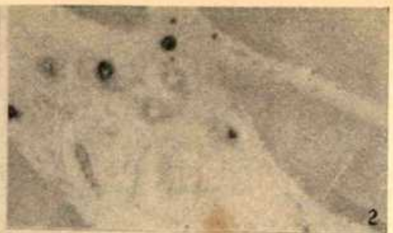
Human Muscular Dystrophy as an Aberration of the Connective Tissue

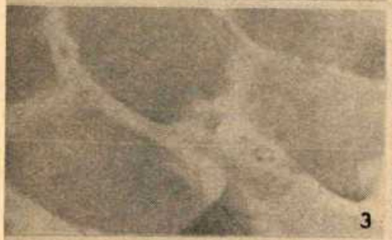
The pathological changes in the muscle in human muscular dystrophy have been well characterized. They consist of great diversity of muscle fibre size, increase in number of sarcolemmal nuclei (which may take the form of chains situated centrally in the fibre), and atrophy of the fibres. Although it has been said[1] that phagocytosis of degenerating fibres is rare, we have found evidence in a number of cases of what appears to be invasion and destruction of muscle fibres by elements of connective tissue.

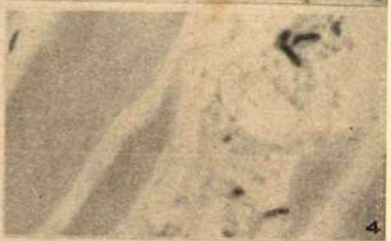
Muscular dystrophy is also characterized by a proliferation of the connective tissue with the accumulation of varying amounts of fat.

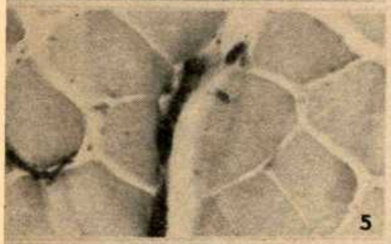
It has been shown by histochemical methods[2] that this connective tissue contains appreciable 5-nucleotidase activity, whereas very little of this activity is present in the connective tissue of normal human muscle. Since this enzyme dephosphorylates adenosine monophosphate, we investigated the ability of the connective tissue to dephosphorylate various high-energy phosphates derived from adenosine monophosphate and other esters and also some other phosphate compounds of physiological importance.

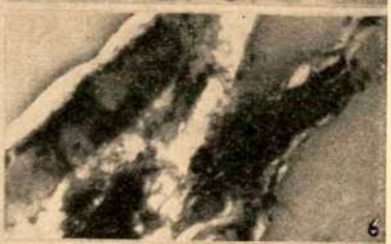


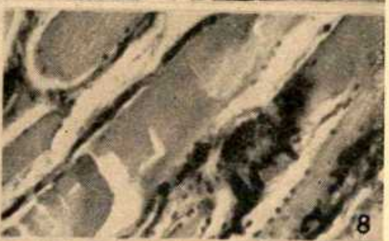


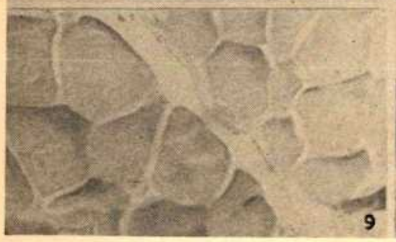












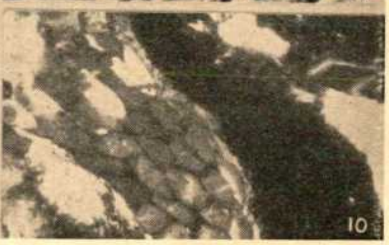


Fig. 1. Substrate: Glucose-6-phosphate. Control muscle, pH 9. Reaction only in one capillary. Connective tissue negative

Fig. 2. Substrate: Glucose-6-phosphate. Dystrophic muscle, pH 9. Reaction only in small blood vessel. Connective tissue negative

Fig. 3. Substrate: Creatine phosphate. Control muscle, pH 8·5. All elements negative

Fig. 4. Substrate: Creatine phosphate. Dystrophic muscle, pH 8·5. Slight reaction in some capillaries. Connective tissue negative

Fig. 5. Substrate: Adenosine triphosphate. Control muscle, pH 9. Some capillaries and muscle nuclei positive. Connective tissue negative

Fig. 6. Substrate: Adenosine triphosphate. Dystrophic muscle, pH 9. Intense reaction by proliferating connective tissue elements. The reactions given in 5 and 6 are by a heat-stable adenosine triphosphatase which appears to be different from the conventional adenosine triphosphatase of the muscle fibre

Fig. 7. Substrate: Triphosphopyridine nucleotide. Control muscle, pH 9. All elements negative

Fig. 8. Substrate: Triphosphopyridine nucleotide. Dystrophic muscle, pH 9. Considerable reaction by elements of proliferating connective tissue and muscle nuclei

Fig. 9. Substrate: Thiamine pyrophosphate. Control muscle, pH 7·5. All elements negative

Fig. 10. Substrate: Thiamine pyrophosphate. Dystrophic muscle pH 7·5. Spectacular dephosphorylation of proliferating connective tissue and moderate reaction by muscle fibres

They included adenosine di- and tri-phosphates, uridine, guanosine, cytidine, inosine and acetyl phosphates and creatine phosphate. Phosphorylated co-enzymes such as riboflavin-5-phosphate, thiamine pyrophosphate, pyridoxal phosphate, di- and triphosphopyridine nucleotides and glycolytic intermediates such as glucose-1- and glucose-6-phosphates, fructose-1- and 6-phosphates, hexose diphosphate and phosphoglyceraldehyde. The histochemical reactions for all these compounds were compared with that for β-glycerophosphate. Our studies in 10 cases of muscular dystrophy showed that in every case, with the exception of creatine phosphate, all the high-energy phosphate compounds were actively dephosphorylated by the connective tissue and by a number of the muscle fibres. On the other hand, the intermediate glycolytic compounds were not hydrolysed. Of the co-enzymes, riboflavin-5-phosphate and pyridoxal phosphate were not affected, but in two out of the ten cases of dystrophy there was a spectacular dephosphorylation of thiamine pyrophosphate. Probably the most interesting result was the dephosphorylation of diphosphopyridine nucleotide and to a lesser extent triphosphopyridine nucleotide by the connective tissue in every case examined.

The presence of enzymes destructive of compounds vital to muscle metabolism in connective tissue enveloping the muscle fibres must have some significance in muscular dystrophy.

There are three possible interpretations of these observations:

(1) Although these metabolically important phosphate compounds are synthesized by muscle there may be some leakage in normal metabolism much as vitamin A leaks away from the retina in the retinene cycle. Replacement of this leakage by transport from the vascular and lymphatic system if there is inadequate synthesis by the muscle itself would be prevented by connective tissue containing the appropriate phosphorolytic enzymes.

(2) The fundamental defect may still be in the membrane of the muscle fibres, and the diffusion of phosphate esters out into the surrounding milieu may result in adaptive synthesis of enzymes to hydrolyse them in the connective tissue.

(3) That the excessive production of these hydrolytic enzymes by the connective tissue leads to their diffusion to and adsorption on to and eventual penetration of the muscle fibre membrane resulting in complete block of the normal metabolism of the fibres.

Of these possibilities (2) is currently under investigation in this laboratory, and of (1) and (3) the latter appears to be more in keeping with current views of muscle metabolism although the penetration of the sarcolemma by hydrolytic enzymes has yet to be established. However, it does not seem improbable that the accumulation of such a range of phosphatases at this site might break down both its structural integrity and its selective permeability.

These results suggest that the fundamental defect in progressive muscular dystrophy may be not in the muscle fibre but in the connective tissue which supports it.

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Chemical Changes in Human Bronchial Epithelium and their Relation to Bronchial Cancer

A RECENT histological study[1] of the changes that occur in human bronchial epithelium has confirmed in part earlier American findings[2] and shown that considerable proliferation may occur in the cells of the basal layer without any other histological abnormality. As it seemed possible that some of these changes might be related to the development of bronchial cancer, a histochemical investigation has been begun. Since this work was not concerned with the distribution of free lipids, formalin-fixed tissue embedded in paraffin was used. The most striking result has been the very marked increase in the content or availability of lipid, probably bound phospholipid[3], as shown by colouring with sudan black and staining by the acid hæmatein method[4]. This effect was strongest in the nuclei of the basal cells and was particularly well seen in the condition known as basal cell hyperplasia. In contrast, scarcely any lipid could be demonstrated in the cells of foci of established squamous metaplasia.

Since basal cell hyperplasia and other proliferative changes are common in smokers who exceed 40 cigarettes a day, it seemed worth-while to see if similar histochemical disorders occurred in histologically normal areas of bronchial epithelium in such persons. By these methods an increased lipid content has now been demonstrated in the basal cells, particularly in the nuclei, of otherwise normal bronchial epithelium from such smokers; in chemically normal epithelium from non-smokers only the nucleoli in the basal cells are stained.

Sections were also treated with an aqueous (hydrotropic) solution of 3,4-benzpyrene, and the distribution of this fluorescent carcinogen was followed by fluorescence microscopy. Those cells which gave a positive reaction with the acid hæmatein method also showed selective absorption and concentration of benzpyrene, especially into the nuclei.

If these observations on fixed cells can be related to events in the living epithelium, they would suggest the possibility that bronchial cancer is produced in two main stages. In the first stage, damage to areas of epithelium, possibly by cigarette smoking, might alter them in such a way as to increase their affinity for lipid-soluble substances, leading to preferential absorption of carcinogenic hydrocarbons in the second stage. These events need not necessarily occur in every focus of proliferation, and the development of bronchial cancer might also be affected by local differences in the concentration of carcinogens which accumulate in the vicinity of the foci. The circumstances influencing the local concentration of carcinogens are probably complex and include such factors as stagnation of mucus and loss of cilia.

We acknowledge, with much gratitude, the generous help given us by Dr. E. Nassau and Mr. R. F. Cummings, of Harefield Hospital, Middlesex. We are also indebted to the Imperial Cancer Research Fund, which has financed these investigations.

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BIOLOGY

Selective Staining of Visceral Efferents in the Rat Brain Stem by a Modified Koelle Technique

THE histochemical technique for cholinesterases introduced by Koelle and Friedenwald[1] has been used in numerous studies of nervous tissue. Much of this work has been concerned primarily either with the histochemistry of the method or with the cytological distribution of enzyme revealed. This method has, we feel, also great potentialities in the field of neuro-anatomy—as a means of selectively staining particular groups of neurones which cannot otherwise be distinguished by more conventional methods. Some attempts along these lines have been made in studies of peripheral innervation[2,3], but it is in studies of the central nervous system that there is particular need for a selective staining method. This communication is therefore concerned not so much with enumerating our detailed findings in this preliminary investigation as with emphasizing the potential value of this technique in solving many neurological problems which have so far resisted attack by more conventional methods.

The sensitivity of the Koelle technique can be controlled by varying the *p*H of the incubation medium and the time of incubation. At an acid *p*H the method is highly selective for sites of high enzyme activity. This fact was made use of by Snell and Garrett[4] in their study of the cholinergic innervation to the rat salivary glands—the secretor-motor fibres, both pre- and post-ganglionic[3], being selectively shown up when a sufficiently acid incubation medium was used. This work suggested that it might be possible with some such technique to follow the salivatory pathway back to the salivatory nuclei in the hind

Table 1. OBSERVED SITES OF INTRACELLULAR STAINING
(In approximate descending order of intensity)

Caudo-ventral portion of sensory nucleus of V
Dorsal motor nucleus of X
Salivatory nucleus
Nucleus of the locus coeruleus
Nucleus ambiguus
Branchiomotor nuclei of V and VII
Pontine nuclei
Giant cells of Deiters and Bechterew nuclei
Some giant cells of medial reticular formation
Somatic motor nuclei of VI and XII

Table 2. FIBRE TRACTS STAINED

Strongly stained

Visceral efferents of X
Nervus intermedius, dorsal and ventral roots
Dorsal decussation in region of facial colliculus

Moderately stained

Fibres accompanying dorsal root of nervus intermedius but apparently entering VIII
Fine fibre bundle within descending limb of VII and apparently forming major part of dorsal decussation

Weakly stained

Branchiomotor efferents of V and VII
Ponto-cerebellar fibres (brachium pontis)

brain, the exact site of which was uncertain. In the rat, this possibility appears to have been realized.

The precise procedure which finally proved to give the best results for our immediate purpose was, very briefly, as follows. The relevant region of the hind brain was dissected out, fixed in cold 10 per cent formol-saline and then well washed in water. Serial transverse sections were cut at 40μ on the freezing microtome and the individual sections treated by the Koelle technique with a *p*H of 4·8–4·9 and an incubation time of about 3 hr. The sections were then mounted serially on glass slides, allowed to dry and afterwards mounted in balsam via absolute alcohol and xylene. These sections were not counterstained in any way: instead they were compared with several companion series of wax sections which had been stained in other ways (Bodian, modified Weigert, cresyl violet).

The brain-stem structures which showed significant staining by this technique are listed in Tables 1 and 2. The patterns of staining seen in and around individual cells were of three main types. Staining confined to the cell bodies and their processes was seen in the caudo-ventral portion of the sensory nucleus of V, in the dorsal motor nucleus of X and in the nucleus of the locus coeruleus. At most of the other sites listed in Table 1 there was significant staining also outside the cells which was most marked in the salivatory nucleus and in the nucleus ambiguus. The third type, in which staining was confined to small discrete areas of the cell surface, was less frequently seen and was most obvious in some of the giant cells of the reticular formation. One is tempted to suggest that each of these three types of pattern represents a different type of synaptic junction: the first, cholinergic neurones receiving mainly non-cholinergic presynaptic terminations; the second, cholinergic neurones which either receive significant cholinergic innervation from elsewhere in the central nervous system or possess recurrent collaterals; and the third, non-cholinergic neurones which receive some cholinergic innervation.

The difference in the intracellular staining of the various types of motor cells and of their processes was very striking. In general, visceral efferents were strongly stained, branchial efferents moderately and somatic efferents only weakly stained. These results imply that the enzyme activity possessed by these three classes of cholinergic neurons must be markedly different, though why this should be so is not immediately obvious. Whatever the underlying reasons, however, the heavy differential staining of the salivatory efferent fibres made it possible to establish their cells of origin with reasonable certainty. It has been generally supposed that there are two salivatory nuclei, an 'inferior' and a 'superior', both situated in the lateral reticular formation. In our material, however, the fibres of the nervus intermedius could be traced via two roots to a dorso-medially placed salivatory nucleus, in series with the Edinger-Westphal nucleus and the dorsal motor nucleus of X. The nucleus is subdivided by the anterior genu of VII into a larger lateral and a small medial part. These two parts of the salivatory nucleus are connected across the top of the genu by strongly stained fibres but not by cells. Some fibres, presumably from the medial part, cross the midline. There is no inferior nucleus in the region between the salivatory nucleus and the dorsal motor nucleus of X, but a fibre bundle leaves the more ventral root of the nervus intermedius to join the efferent outflow of IX. No salivatory cells can be seen in the traditional site for the superior nucleus in the lateral reticular formation. This more dorsal position for the salivatory nucleus does not conflict with most of the available physiological evidence. It is strikingly consistent with the result of stimulation experiments on the monkey[5] and on the cat[6]: so it is probable that our findings in the rat hold for other mammals.

The observations mentioned here, particularly those relevant to possible central salivatory pathways, will be described and discussed in greater detail elsewhere.

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Fate of Spermatozoa penetrating into the Tissues of the Fallopian Tube

IN a re-investigation of previous work[1], spermatozoa were recently observed in the mucous membrane of the Fallopian tubes of greater horseshoe bats[2], and a similar occurrence was later found in common pipistrelle bats, rats, stoats, one rabbit, and one hedgehog[3]. There was some evidence of a response of the nuclei of the tubal cells to the spermatozoa[3]. In view of these observations, we have examined the Fallopian tubes of mice mated to radioactive males known to be ejaculating large numbers of spermatozoa labelled in deoxyribonucleic acid with adenine-8-^{14}C[4]. By using autoradiography, the labelled sperm chromatin can be identified even though the spermatozoa are no longer recognizable morphologically[5]. The Fallopian tubes were accordingly examined autoradiographically. Particular attention was paid to the mucosa and sub-mucosa, to find out if spermatozoon deoxyribonucleic acid was incorporated into the nuclei or formed nuclei in the female tract.

The Fallopian tubes of five mice were examined in detail. Four of them had been autopsied 12 hr. after mating, the fifth 24 hr. after mating. Many labelled spermatozoa were found between the nuclei of the mucosal cells, which is to be expected from previous work[1-3], though the displacement of some of these spermatozoa during sectioning[6] is possible. Three autoradiographs in the animal killed 24 hr. after mating were associated with sperm heads that appeared swollen and possibly disintegrating. Several thousand nuclei in the mucosa and sub-mucosa were examined, and none was found to give a definite autoradiograph.

Our evidence indicates that spermatozoa do not form nuclei in the mucosa or contribute detectable amounts of deoxyribonucleic acid to mucosal cell nuclei in the Fallopian tubes. Though the chance of detecting nuclear autoradiographs depends on the percentage of spermatozoa that are labelled, the intensity of labelling[4], etc., sufficient numbers of nuclei were examined to exclude the possibility of large-scale participation of male chromatin in them. Our results do not preclude the possibility of the entry of some components of spermatozoa into nuclei, for the intensity of labelling is more favourable to the detection of whole spermatozoon heads than to parts of them. While not ruling out the possibility of xenia, telegony or other effects of the excess spermatozoa in the female tract (see refs. 1, 7), our present results support previous findings[8], which gave no evidence to support theories of these phenomena based on the incorporation of spermatozoa into tubal or uterine cells.

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Electron Microscope Observations on the Neurohypophysis of the Ferret

We have observed, while studying the neurohypophysis of the ferret using the electron microscope, that the mitochondria in the neurosecretory fibres are of unusual form and that this form can be modified by experiment.

The features we have observed are evident in specimens fixed either by buffered osmium tetroxide or by buffered potassium permanganate, though they are more obvious after the latter fixative.

The mitochondria are irregular in form, and in many instances one or more deep invaginations are present (Fig. 1). In permanganate-fixed preparations the area contained within an invagination is strikingly less electron-dense than the rest of the cytoplasm, and we believe that this may indicate a concentration of some specific substance produced by, or involved in, the activity of the mitochondrion.

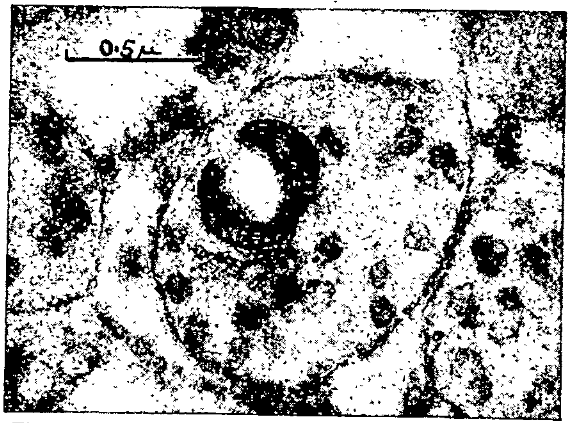

Fig. 1. A nerve fibre in the neurohypophysis of a ferret. It contains neurosecretory vesicles and a single invaginated mitochondrion. The area of the invagination is less electron-dense than the surrounding cytoplasm. The tissue was fixed in buffered potassium permanganate

The pituitary stalks of some animals were severed and the neurohypophysis was examined at various intervals after the operation. Up to four days after stalk section the only apparent effects of the operation were changes in the form of the mitochondria. These continued to be irregular; but the invaginations were less marked and were very rarely associated with any area of electron density different from the rest of the cytoplasm. We interpret this as evidence of some alteration in the activity of the mitochondria following section of the stalk.

A parallel series of histochemical studies was carried out, using the performic-acid – Alcian blue technique[1] which stains selectively cystine-containing material. Some shrinkage of the neurohypophysis followed section of the stalk, but large amounts of Alcian-blue-positive material persisted for at least four days following the operation. It is interesting to note that the electron microscope showed that neurosecretory vesicles were also present during the post-operative period.

It is widely held that[2,3] the neurosecretory material in the neurohypophysis is elaborated in the hypothalamus and that it then passes down axons in the pituitary stalk. It is interesting to find that such material is still present in the distal part of the neurohypophysis four days after section of the axons.

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The Nematodes *Ostertagia lyrata* Sjöberg, 1926, and *Trichostrongylus longispicularis* Gordon, 1933, in British Cattle

A list of the gastro-intestinal nematodes of British cattle, published by Morgan and Soulsby[1], included two species of *Ostertagia* (*O. ostertagi* and *O. circumcincta*) and three species of *Trichostrongylus* (*T. axei*, *T. vitrinus* and *T. colubriformis*). Observations at Weybridge indicate that an additional species of each of these two genera, namely, *O. lyrata* and *T. longispicularis*, should be added to this list.

These two species were present in material collected during the routine post-mortem examination of bovines which were suffering from parasitic gastroenteritis, and which had been sent to the Laboratory from farms in the south-east of England. *O. lyrata* together with *O. ostertagi* was recovered from the abomasum, and *T. longispicularis* together with

Cooperia spp. and *Nematodirus* spp., was recovered from the small intestine.

O. lyrata can be differentiated readily from *O. ostertagi*, and from *O. circumcincta*, which also occurs in the abomasum, as the copulatory bursa and spicules are characteristic for each species[2]. Differentiation of the *Trichostrongylus* species is more difficult, *T. longispicularis* and *T. colubriformis* being very much alike. In both species the spicules are the same general shape, except at the tips, but those of *T. longispicularis* are slightly longer than those of *T. colubriformis*. The gubernaculum, however, is quite distinctive for each species and provides an additional means of differentiating the two.

O. lyrata has been recorded from cattle, sheep and deer. It is known to occur in Europe, North America and Africa. According to Becklund[3] it is a fairly common cattle parasite in Georgia, U.S.A.

T. longispicularis has been recorded from both sheep and cattle in Australia and North America. It is said to be fairly common in cattle in certain parts of Australia[4].

There is no experimental evidence relating to the pathogenicity of either *O. lyrata* or *T. longispicularis*. It seems reasonable to suppose, however, that heavy infestations will have harmful effects on the host similar to those produced by other species of *Ostertagia* and *Trichostrongylus*.

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Food Selection by Silkworm Larvæ

THIS communication reports the presence of three stimulants in mulberry leaves which induce their preferential selection as food by silkworm larvæ. The first, which attracts the larvæ on to these leaves, has been identified as β,γ-hexenol or α,β-hexenal by T. Watanabe[1]; the second, which stimulates biting action, occurs in the methanol-soluble fraction of the leaves; and the third, which appears to stimulate continuous swallowing by the larvæ, is present in the fraction insoluble in methanol and soluble in water. A combination of these factors is of importance for the positive acceptance of food by silkworm larvæ. By the use of these stimulants, extracted chemically from mulberry leaves, larvæ have been induced to feed on agar.

The stimulant for biting action was first discovered in water- or methanol-extracts of young mulberry leaves, picked on a fine day, whereas in older leaves this stimulant was found to exist in an insoluble form.

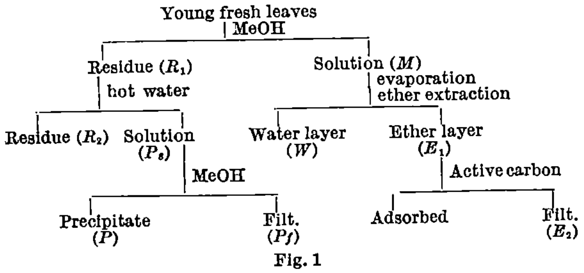

Fig. 1

Young mulberry leaves were extracted with several solvents and fractionated (Fig. 1). For the test of biting action, agar in its original state as threads was soaked in these fractions and then used as a test for biting action. In this state the agar is not soft enough to be bitten off and swallowed, so that the biting reaction can be observed on its own. Table 1 shows whether or not each fraction was observed to be a stimulant for biting action. It will be seen that the methanol-soluble fraction (M) contains this stimulant. After treating this fraction with ether, reduced activity of stimulant was observed in both ether fractions (E_1 or E_2) and in the residual water layer (W), but the total activity was recovered by mixing these two fractions. The purified ether-soluble active fraction (E_2) is a yellowish syrup with a peculiar odour.

Table 1. TESTS OF BITING ACTION

Fraction	Reaction
M	+ + + + +
R_1	+ + + + +
W	+ + + − −
E_1	+ + + − −
E_2	+ + − − −
$E_2 + W$	+ + + + +
P_s	− − − − −
R_2	+ − − − −

To test for the continuous swallowing reaction, the modified method of Thorsteinson[2] was used. That is, 3 per cent agar solution containing 1 per cent sucrose and 5 gm. of filter-paper powder was used as basal substrate. The addition of this paper powder, which enabled the larvæ to produce fæces similar to those of larvæ fed on leaves, made the test quantitative. Each fraction was added to agar basal substrates. The numbers of fæces produced overnight was taken to indicate the degree of stimulation of the swallowing action (Table 2). There was no significant difference between the numbers of fæces in experiments 1 and 2, indicating that the basal substrate was suitable for this test and that dried leaf powder may be used in place of fresh leaves. In the case of the basal diet itself, basal diet with pectin (P) or extract residue (R_2), the silkworms did not try to bite the agar at all, as shown in experiments 9–11.

Table 2

Experiment No.	Substrate	Total No. of fæces	Fæces on agar
1	Leaf powder (5 gm.)	204	156
2	Fresh leaves (10 gm.)	199	0
3	M	78	52
4	E_2	36	4
5	$E_2 + P_s$	88	52
6	$M + P_s$	186	144
7	$M + Pf$	182	121
8	P_s	37	5
9	P	40	0
10	Basal diet	27	0
11	R_2 (5 gm.)	21	0

Basal diet: 50 cm.³ of 3 per cent agar solid solution containing 1 per cent of sucrose and 5 gm. of filter-paper powder.

Dosage: Each fraction, M, E_2, P, etc., corresponds in amount to that in 5 gm. of powdered mulberry leaves.

Number of fæces: Five larvæ at the fifth stage were put in a shale overnight at 25° C. and the fæces were then collected.

In experiment 3, and especially in experiment 4, the agar contained only one stimulant for biting action, and larvæ tried momentarily to bite the agar, but did not eat continuously. From these experiments it is evident that another factor is necessary for acceptance of food by the larvæ. In experiments 6 and 7, the silkworms ate the agar continuously as if it were mulberry leaf. The agar in these experiments contained a mixture of the fractions M plus P_s or M plus P_f, respectively. From these experiments, the fractions P_s and P_f seem to contain a stimulant for swallowing action. Fraction P_s is a water-extract of the residue after treating the leaves with methanol, and fraction P_f is obtained from P_s by the removal of pectin. But, as shown in experiment 8, the presence in agar of this stimulant alone is not sufficient for its acceptance as food by the larvæ, as is also the case with the biting factor alone. Moreover, the agar containing both biting and swallowing factors, as shown in experiment 5, is also not acceptable as food. The methanol extract (M) contains a biting factor and also the volatile substances from mulberry leaves, so that in experiments 6 and 7 the agar contained all three stimulants. Thus the presence of the three stimulants is necessary for food selection by silkworms and the absence of any one of the stimulants inhibits feeding by the larvæ.

I wish to acknowledge the advice given in connexion with this work of Dr. G. S. Fraenkel.

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Methods of marking *Tilapia* Spp. (Pisces : Cichlidæ)

VARIOUS species of *Tilapia* form the basis of large commercial fisheries in eastern and central Africa, and *T. mossambica* Peters has now been distributed in almost every tropical region outside Africa for culture in ponds. Simple methods of marking for individual and batch recognition can yield valuable information to such fisheries. Two marking techniques have been developed at the Inland Fishery Research Station of this Ministry during the past eighteen months, using populations of *T. nigra* (Günther) in ponds.

Individual marking. An entirely satisfactory tagging method has been evolved from techniques extensively used by the Scottish Home Department in salmonid studies. The tags are made of coloured plastic strips, 6 mm. × 3 mm., rounded at both ends, with serial numbers and letters die-stamped on either side. A small hole is drilled at one end and the tag mounted centrally with three close twists on a 5 cm. length of 0·0136-in. diameter annealed silver wire. For marking fishes, the dorsal musculature is pierced with a No. 18 gauge hypodermic needle between the roots of the first and second (or second and third) hard dorsal rays, and one end of the wire is threaded into the needle. On withdrawing the needle, the wire is brought through the muscles and the two ends of wire are twisted three or four times together against the body. The free ends of wire are cut short and both tag and securing twist are pressed back against the body of the fish. Pulling the tag tight is important, since loose tags lead to severe wounding.

Between each tagging the needle is dipped in surgical spirit, which appears adequate to prevent any infection. This method of tagging has no effect on subsequent growth, and some fishes so tagged are still alive and growing in ponds eighteen months after marking. Actual increase in length of these fishes has been as much as 20 cm. in the first six months after marking and the tags are firmly and cleanly in place. Several hundred fishes have been tagged thus in the last twelve months, and no casualties attributable to tagging have occurred, though it is not advisable to mark fish below 6 cm. total length.

Loss of tags has never exceeded 8 per cent, despite repeated monthly netting and handling of the fish. In wild populations, or those handled less frequently, the tags are probably lifelong fixtures. There has been no evidence of selective predation of tagged fishes.

This method is now being employed on a large scale for marking *Tilapia* in Lake Victoria, but a modification in this instance has been to insert the tags near the bases of the posterior hard dorsal rays in order to avoid accidental and unselective tangling of the fish, in the gill-nets used, by the ends of wire. We have also marked wild river populations of *Labeo* and *Barbus* species, well-tagged fish of each kind being re-trapped up to eight months later.

Batch marking. Individual tagging is slow (not more than 80 fishes per man per hour), and for rapid marking some form of fin-clipping is preferable. Since in *Tilapia*, dorsal, pectoral and anal fins play a part in epigamic display, only pelvic fins have been amputated; and by simple amputation of these, several hundred fish can be marked per hour. Such amputation has always been made across the proximal bases of the fin rays, since total amputation at the peduncle usually causes excessive bleeding, and may lead to infection.

In almost all cases, clipped fins have regenerated to full size, often in as little as thirty days. In less than 1 per cent of those clipped, no regeneration has occurred, possibly due to complete amputation of the peduncle. After the first month, therefore, immediate recognition of clipped fins is not possible, but nevertheless certain structural differences are apparent macroscopically up to six months afterwards and are by then probably permanent.

Table 1. DELAY IN BIFURCATION OF PELVIC FIN RAYS IN *T. nigra* AFTER FIN CLIPPING: COMPARISON IN A FISH 18·7 CM. AFTER FIVE MONTHS

	Branched rays									
	Left pelvic (cut)					Right pelvic (uncut)				
	1	2	3	4	5	1	2	3	4	5
First bifurcation	55·5	46·3	41·5	42·0	49·2	60·0	41·3	41·8	47·0	42·2
Second bifurcation										
Anterior	—	82·0	70·2	68·5	73·5	—	61·5	54·9	45·8	47·7
Posterior	—	68·5	61·0	66·2	—	—	55·8	55·5	52·0	70·0
Third bifurcation										
Anterior	—	—	—	—	—	—	79·0	82·5	78·0	—
Posterior	—	—	—	—	—	—	—	79·0	—	—
Length of unbranched ray (mm.)			17·0					19·5		
Total length of ray (mm.)	32·7	30·9	26·0	21·0	16·6	32·3	30·5	25·5	21·2	16·8

Figures refer to distance from base of ray to bifurcation expressed as percentages of total length of that ray.

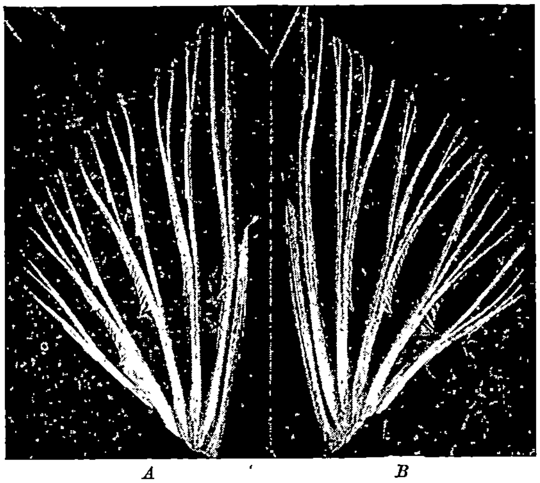

Fig. 1. Pelvic fins of *T. nigra* five months after clipping. *A*, Left clipped pelvic; *B*, right unclipped pelvic

In *T. nigra* the pelvic fin ray formula is *PI* 5. The first branched ray usually bifurcates once only (rarely twice), but the remaining four rays always bifurcate twice, and a third bifurcation may occur in parts of the second, third and fourth ray. In most cases fin-clipping does not alter the formula or number of bifurcations, but the difference between regenerated and normal fins lies in the apparent deferment of the second bifurcation (instead of very shortly after the first) in clipped fins, and possibly as a result of this, the more definite separation of the rays after the first bifurcation. Table 1 gives such differences numerical expression, and from this it is apparent that while the point of first bifurcation is little altered in regenerated fins, the second bifurcation is delayed by about 20 per cent in the anterior branch and 10 per cent in the posterior branch of the ray. This difference is easily recognizable in the field with practice. In addition, the first unbranched (spiny) ray is often slightly shorter in clipped fins, such a slight disparity being apparent even in the live fish on examination if the fins are pulled forward by these spines.

Fish used in these experiments have all shown fast growth in ponds up to 4 cm. per month, the delay in bifurcation and rapid regeneration of the fins perhaps resulting from this, although essentially the same pattern has been found in fish the growth of which has been depressed to 1–2 cm. per month. In wild populations growth may average only a few centimetres a year, and the speed and pattern of regeneration may be different. Nevertheless, the much greater numbers of fish which can be fin-clipped, as opposed to individual tagging, would lead to a higher percentage return of marked fish in commercial catches, if such catches are sampled from time to time by an observer trained to detect such differences.

Amputation of the upper lobe of the caudal fin has also been tried, but in all cases it has completely regrown and shown no structural difference to a normal fin within a month, so that caudal clipping cannot be recommended as a marking technique.

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Seasonal and Tidal Fluctuations in the Trawl Catches from the Sierra Leone River Estuary

In March 1958, a series of fish-marking experiments was initiated for the first time in Sierra Leone territorial waters. Only the demersal species of commercial importance were marked, and the area chosen for the first year's liberations was the trawling ground off Robene Point, some 13 miles from the mouth of the Sierra Leone River estuary. The fish for marking were caught with a 28 ft. or 42 ft. otter trawl towed by a 28 ft. diesel-powered launch. A total of 439 hauls, each of 39 min. duration, was made during the course of the marking experiments.

An analysis of the results of the catch shows that over the whole period of the experiments, from March 1958 until January 1959, an average of 51 per cent of the catch per haul was marked, 33 per cent of the markable fish died during the trawling operation and 16 per cent were unmarkable fish such as *Arius* and *Dasyatis*, dangerous to handle. The results also show a very distinct fluctuation in the catch-rate, which was related to the tidal range—higher catches were made at neap rather than spring tides; there was no obvious relationship, however, between the rate of catch and state of tide.

Table 1. The Average Number of Fish of all Species in Each Haul during the Period March 1958–January 1959

Month	No. of fish per haul	No. of hauls
March	32	56
April	30	41
May	27	51
June	19	17
July	5	30
August	15	31
September	24	43
October	43	54
November	56	34
December	62	26
January	44	56

Table 1 gives the average number of fish of all species caught per haul. In July, a change was made from a 28-ft. to a 42-ft. net, and despite its greater catching power, there is a fall-off in the catch-rate during the wet season (May–October). A similar decline in the catch-rate was observed by two trawler firms operating in the Banana Islands area, 25 miles south of the estuary mouth—a fact which suggests that there may be a general movement of the fish stocks away from the inshore regions of low temperature and salinity at this time of the year.

There are some indications that the catch-rate may also be influenced at times by differences in the opacity of the water masses covering the grounds. Normally the water is very turbid, and Bainbridge[1], using a standard 30-cm. Secchi disk during plankton investigations in the estuary, found greater turbidity at spring than at neap tides, presumably due to the greater scouring action of the very strong (4–5 knot) tidal currents on the ebb at springs. Extinction coefficients (K–1·7/D) of as much as 3·4, corresponding to a disappearance of the disk at only 0·5 m., were recorded in the mid-estuarine region at such times. During the present experiments, observations were made at various states of the tide with a disk of a similar diameter in the Robene Point area. The readings, which have been compared with the catch per haul, are given in Table 2. From these comparisons, it will be clearly seen that there is a fall-off in the catch-rate with the clearer water, presumably due to the fish avoiding the gear. In this connexion,

Table 2. The Relationship between the Opacity of the Water and the Average Catch per Haul in the Robene Point Area during the Period September to December 1958

Secchi disk-range (m.)	Average No. per haul	N.
0·5–0·9	26	18
1·0–1·4	28	23
1·5–1·9	25	33
2·0–2·4	23	40
2·5–2·9	16	18
3·0	>3	4

it is interesting to note that over a five-day period in June, when the water in the Robene Point area was exceptionally clear, a nylon net gave a catch-rate of 110 lb. per hour and a tanned hemp net 33 lb. per hour when fished in turn from the same boat; the difference disappeared when the disk readings fell below 3·5 m.

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The Amphipod, *Hyperia galba*, an Ectoparasite of the Jelly-fish, *Cyanea capillata*

Very few real facts are known concerning the relationships between the amphipod *Hyperia galba* (Montagu) and the various jelly-fish with which it is associated. Some writers have referred to *H. galba* as a parasite[1–4] but without providing any direct proof. Orton[5] assumed *H. galba* to be a food parasite, and Hardy[6] was inclined to accept this view. Stephensen[7] maintained that no amphipod except the cyamids is a true parasite, and this is the view adopted in current parasitological works of reference.

Recently, I had the opportunity to examine histologically the digestive tract of twenty-five specimens of *H. galba* from Bergen, Norway, which were obtained from *Cyanea capillata* (L.). I was immediately struck by the presence of empty nematocysts in virtually all the formed food remains encountered in the gut. As *C. capillata* frequently catches other medusae, especially *Aurelia aurita* (L.) and hydromedusae, it remained to settle whether the nematocysts came from *C. capillata* itself or from its prey. Few nematocysts pass the mouth-parts of *H. galba* undamaged, but in one specimen a number of well-preserved, discharged nematocysts were found in the atrium oris. Several of these nematocysts could be identified as heterotrichous microbasic euryteles of the type characteristic of scyphozoan medusae. Three of them which could be accurately measured were 13·2, 13·4 and 14·1μ long and 8·6, 8·6 and 9·4μ wide, respectively. Papenfuss[8] gives the average of 50 discharged euryteles of *C. capillata* as 13·6μ × 8·1μ and the normal (length ?) variation as ± 2μ. Thus the three nematocysts in question fall well within the normal range of *C. capillata* but outside that of all other scyphozoan medusae occurring in the area. One further discharged nematocyst could be identified as a haploneme measuring 17·0μ in length × 11·2μ in width. Nothing can be seen of any possible armature of the thread. The size agrees fairly well with that of the atrichous haploneme *A* of *C. capillata*, which averages[8] 18·0μ × 13·2μ. Although the hundreds of empty nematocyst capsules found in the gut cavity could not be accurately measured, they give the same general impression as a slide of macerated nematocysts of *C. capillata*, while a similar sample from *A. aurita* looks rather different, the capsules being much smaller. A very small number of nematocysts pass the intestine undischarged. Generally, they are rather distorted, and in no case has it been possible to measure them with satisfactory accuracy. Some of them could be identified as euryteles.

On the evidence presented above, it seems safe to conclude that *H. galba* is a true ectoparasite of the jelly-fish with which it is associated. A more comprehensive account of the observations will be published elsewhere.

The material for the present study was collected at the Marine Biological Station of the University of Bergen.

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Evidence on Growth-rates obtained from Two Marked Humpback Whales

Recent estimates of the age at which whales reach sexual maturity have depended primarily on the interpretations placed on the rate of accretion of recognizable zones in certain structures such as baleen and ear plugs. Several workers[1,2] have pointed out that none of the ageing methods for any species has yet been standardized against organs from whales of known age. Only whales marked as calves would be of accurately known age at the time of capture, but no such animals have yet been recovered. However, two marked humpbacks caught in Cook Strait, New Zealand, have each provided material from immature animals of known minimal age.

A male humpback (mark No. 12092), was marked in Foveaux Strait, 46° 25′ S. on November 7, 1955, when it was travelling southwards, presumably towards the antarctic feeding grounds. At the time of marking it was estimated to be 36 ft. in length, a figure which later proved too high yet confirmed that the whale was not one of the young suckling calves often encountered in Foveaux Strait[3] at the time of southward migrations. It is therefore very probable that this animal had been born in the subtropical or tropical breeding areas not later than the second winter preceding its marking, and it would therefore have been in its second year at a minimum at the time of marking. On recovery at Cook Strait when it was northbound 19 months later[4] (June 18, 1957) this specimen could be assigned a minimum age of 3 years. The baleen showed three well-defined zones (Fig. 1) consistent with the now generally accepted

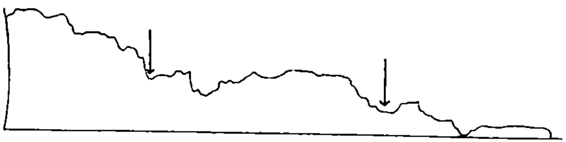

Fig. 1. Baleen tracing from a male humpback of 34 ft. 7 in. showing the three zones regarded as annual increments

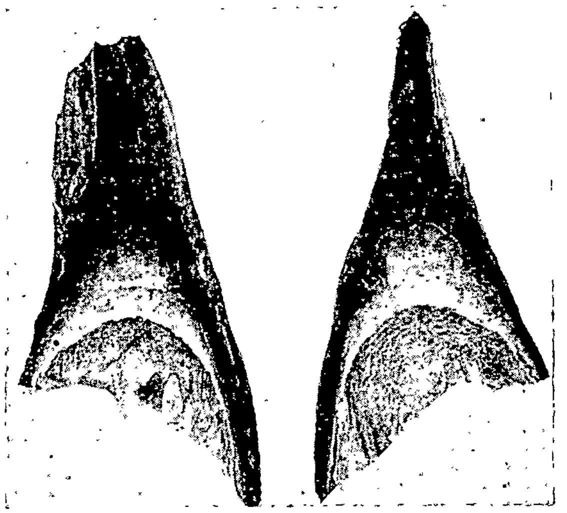

Fig. 2. Section of wax ear plug from the same animal as in Fig. 1. Five distinct and indistinct zones are present

view that baleen adds one zone annually. The wax ear plug, which was rather soft, showed 5 distinct and 2 indistinct laminations (Fig. 2), which agrees satisfactorily with the hypothesis that two ear-plug laminations are formed per year.

The standard length of this humpback at the date of capture was 34 ft. 7 in., and the mean weight of the testes was 1·36 kgm., that is, 0·64 kgm. less than the mean weight of 2 kgm. at sexual maturation[5]. In addition the seminiferous tubules were still closed. While the length at which sexual maturity occurs in male humpbacks off West Australia has been shown to be 36 ft. 9 in.[5], I have found that results from 336 males caught from the same New Zealand stock as that from which this marked specimen was recovered indicate a mean length of 38 ft. 0 in. at this stage. Only three males of less than 37 ft. have been found mature in New Zealand catches while four exceeding 39 ft. were immature, so it is clear that the marked animal was substantially smaller than the size at which sexual maturation is normally achieved. When considered in conjunction with the size of testes and closed seminiferous tubules, these results indicate that the marked humpback would have been very unlikely to reach sexual maturity during the following few months in subtropical waters. However, it could possibly have matured during the subsequent winter, 12 months later, when it would have been a minimum of four years old.

A northbound female humpback was marked in Cook Strait (No. 12043) on May 31, 1955. The phase of migration and the fact that it was not a calf indicate that the animal was then at a minimum age of approximately one year. On recovery in Cook Strait exactly 12 months later this whale was 36 ft. in length, with a total ovary weight of 330 gm. While Chittleborough[6] found a mean length of 38 ft. 6 in. for female humpbacks at sexual maturity off west Australia, 426 pairs of ovaries from New Zealand catches examined by me indicate a mean length of 39 ft. 6 in. in the latter region, where only three females of less than 39 ft. 0 in. have proved to be sexually mature, with six females between 41 ft. 0 in. and 42 ft. 6 in. still sexually immature. While there is much individual variation in ovary weights, those from the specimen under discussion were approximately half the weight of the smallest pair listed for a mature humpback[7], and the maximum follicle sizes (18 and 22 mm.) were substantially less than the 30 or more mm. which normally indicates approaching follicle maturation. Follicles of similar sizes to the above have been encountered by Chittleborough[7] in female humpbacks as small as 33 ft. The available results nowhere indicate the approach of sexual maturity within the breeding season commencing at the time the animal was caught. Since the whale would have been at least three years old at the subsequent breeding season, a minimum of three years appears to be required to reach sexual maturity. This figure would have to be raised if the animal was (*a*) more than a year old when marked, (*b*) more than one year under the age at which it would have been mature, or both (*a*) and (*b*). Baleen and ear plugs were unfortunately not obtained from this whale.

The age of sexual maturation indicated by the histories of these two marked humpbacks is substantially greater than the estimate of two years[8] which has long been accepted, but falls within the estimate of 3–4½ years for females[2] calculated after analysis of recent material using indirect methods. No recent estimate for male humpbacks appears to have been published, but the minimal figure of 4 years indicated by the marked whale here described is double that obtained by Matthews[8] for both male and female humpbacks.

Thanks are due to Mr. G. T. Perano and Mr. C. Huntly for material and information relating to the above whales and to Dr. R. G. Chittleborough for preparing the baleen tracing and for his helpful comments on this and the wax ear plugs.

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Genal Cæca of Agnostids

Genal cæca are lateral appendages of the stomach of trilobites and are interpreted as hepatic glands. These glands are not fossilized but are preserved as delicate imprints of veins in the trilobite test. Genal cæca have been found in many trilobites, especially in Cambrian ptychopariids. In agnostids, however, genal cæca have not been described as yet.

In many agnostids (Fig. 1) the surface of the cheeks is wrinkled. The wrinkles form a coherent radiating 'ornament' of narrow furrows—scrobicules, and wider branching swellings—the rugæ. Each cheek has a ramified leaf-like set of rugæ which represents a symmetrical pair of alimentary glands. These glands are homologous with the genal cæca of other trilobites. In agnostids they are connected with the stomach by one pair, or two pairs, of short diverticular ducts. The scrobicules, which are furrows on the outer surface of the test, represent parietal septa on the inner surface. These septa, with

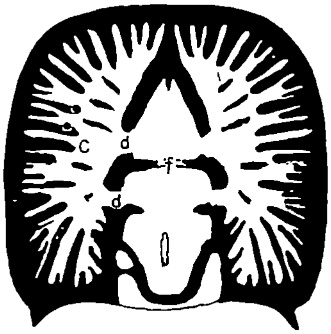

Fig. 1. Cephalon of a Middle Cambrian agnostid (*Ptychagnostus*). *C*, Cæcal glands; *d*, diverticular ducts; *f*, transverse glabellar furrow. Parietal septa (scrobicules), dorsal furrows, and border are shown in black; the cæcal glands, diverticula and bipartite stomach (glabella) are left white

mesenterial membranes attached to them, served as partitions to keep the glands in position. The stomach was located in the glabella, as in other trilobites, but in the agnostids was divided by the transverse glabellar furrow into two connected cavities.

The pattern of the cæcal glands of agnostids is simpler than that of other trilobites and has a great similarity to the cæcal glands of such arthropods as *Burgessia* Walcott and *Naraoia* Walcott. It should be noted that the pygidia of agnostids were provided with similar glands.

Intestinal appendages have been observed as impressions on the test of the thorax and the pygidium in Australian Cambrian ptychopariids as well. It is already evident that the intestinal appendages of trilobites had a segmental distribution and that each segment had two pairs of them.

A full account will be given in a forthcoming paper. This communication is published with the approval of the Director, Bureau of Mineral Resources Geology and Geophysics, Department of National Development, Canberra.

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Life Span of Individual Yeast Cells

THE division of a yeast cell by budding gives rise to two cells which are identifiable, that is, the mother cell from which the bud arose, and the daughter cell which developed from the bud. The wall of the daughter cell presumably is synthesized *de novo* while that of the mother cell retains all or at least part of its identity through the division—an example of linear inheritance[1]. That the wall of the mother cell is not reformed is evidenced by the accumulation of scars associated with each budding event[2]. Electron micrographs[3-5] reveal a scar area that is approximately 1 per cent of the surface area of the cells. If, as indicated by Barton[2], a bud is never formed at the site of a scar, then it is possible that the life-span of individual cells would be limited by depletion of available budding sites. Barton observed one cell to bud 23 times but did not observe a cessation of budding. Other progressive changes also might limit the number of divisions that a single cell can complete. This report describes an experiment designed to determine the life-span of single yeast cells and includes consideration of possible mechanisms for life-span limitation.

A hybrid diploid culture of *Saccharomyces cerevisiae*, *X*30, was used for the entire study. The procedure of life-span analysis was as follows:

A layer of growth medium (0·5 per cent yeast extract, 1 per cent dextrose, 2 per cent agar) was spread on the surface of a 22 mm. × 22 mm. coverslip and a loopful of a dilute suspension of cells was streaked along one edge of the surface of this agar layer. The coverslip was then inverted over a micromanipulation chamber, maintained at 30° C.

With the aid of a micromanipulator, a number of budding cells were drawn into the central region of the agar. The coverslip was then removed, and the agar containing the original inoculum was cut off leaving only the selected budding cells. The coverslip was again placed in position, and the orientation of the buds on each of the mother cells was recorded. The cells developing from these buds were used as starting mother cells and the original mother cells were drawn to the edge of the agar layer. As new buds appeared on the starting mother cells, their positions were recorded, and when they had budded again they were removed. Only when the mother cell and its daughter have each budded can they be separated[6], so bud removal was always delayed one generation. A strip of agar containing the discarded cells and their descendants was periodically cut away from the main agar layer to limit the rate of depletion of the medium. To estimate generation times, the starting mother cells were examined at frequent intervals and the times of appearance of buds recorded. Each of the starting mother cells was followed until it failed to bud further. The total number of buds produced was considered the life span.

A total of 36 mother cells was observed, and the number of buds each produced is shown in the histogram (Fig. 1). A mean life-span of 23·9 generations with a standard deviation of 8·3 generations applies to this distribution. After three or four generations the mother cells were easily distinguished from their mature buds. They were considerably larger than first-generation mother cells, as observed previously[3]. Also surface irregularities that were

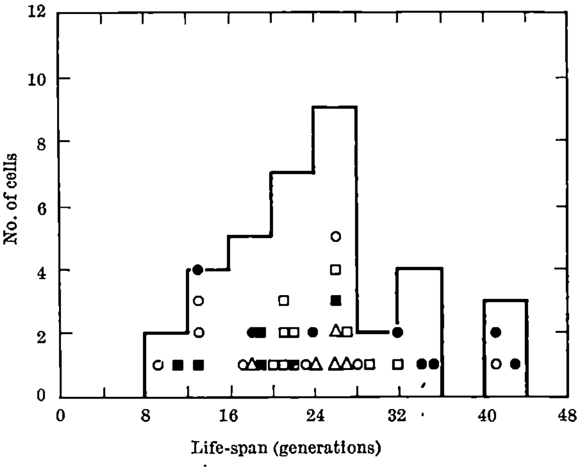

Fig. 1. Life-span distribution for single yeast cells. The different symbols represent separate experiments, except for the open and closed circles. The starting mother cells of the latter series (●) were derived from the first buds of the starting mother cells of the former (○)

most likely due to bud scars were easily seen. Throughout most of the life-span of the cells, the generation time varied between 60 and 100 min. However, the final one to three divisions of nearly all the cells were found to be much longer in duration, some lasting up to 6 hr. With cessation of budding, most of the cells became granular and some lysed. Both of these observations indicate death of the cell.

That the surface area of the cells increases with repeated budding suggests that the bud scar does not replace a portion of the original cell wall but instead fills a region that has been opened in the cell wall during bud formation. If this is the case, limitation of life-span by depletion of available regions for budding would seem less attractive as a hypothesis. Also it would be difficult to account for the wide range of life-spans observed on the basis of this hypothesis. If it is assumed that the scar regions are not active in metabolic exchange between the cell and its environment, a possible explanation of the results could be that the active surface-to-volume ratio decreases below a level necessary to maintain normal metabolic processes, thus precipitating death of the cell. The very long terminal divisions could easily be accounted for on the basis of this hypothesis.

Alternative hypotheses based on random occurrence and accumulation of deleterious nuclear events such as nondisjunction or recessive lethal genetic changes, or on random depletion of essential autonomous cytoplasmic constituents, were considered less plausible since the original population should already be in equilibrium with such events, and the death-rate per generation would be expected to remain constant.

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SOIL SCIENCE

Swelling of Clay–Water Systems

CLAY–WATER systems are such that care must be taken to distinguish between systems which describe the final reproducible hysteresis loop and those systems which can be regarded more appropriately as having a gel-like structure.

In a series of papers, Bolt *et al.*[1–3] have reported film thicknesses for clays saturated with sodium or calcium ions. Their results have been obtained in the main by the drying of clay materials from the gel state. Croney and Coleman[4] and also Holmes[5] have clearly demonstrated that in order to obtain the final reproducible hysteresis loop for a clay material it must be dried to its shrinkage limit. Even after drying to a terminal pressure approaching 40 atm., the water content obtained by Warkentin, Bolt and Miller[3] for a Ca^{2+} montmorillonite, on rewetting to a hydrostatic suction of 0·1 atm., is still extremely high. Water contents obtained in this laboratory using Ca^{2+} montmorillonite (Redhill, Surrey) compressed into cores at 1,200 atm., then taken through wetting and drying cycles from 0·01 atm. suction to complete desiccation over phosphorus pentoxide to obtain the final reproducible hysteresis loop are very much less than those obtained by the workers at Cornell University. Furthermore, in calculating the film thicknesses from their data, these authors have assumed that the water retained by the clays was uniformly spread over the entire surface of the montmorillonite. Thus these workers regarded the internal and external surfaces of the montmorillonite crystals as being equivalent. However, Norrish and Quirk[6] have shown that for Ca^{2+} montmorillonite the $d(001)$ spacing does not increase beyond 19 A., which indicates a film thickness considerably less than the overall film thickness calculated by Warkentin, Bolt and Miller.

Before proceeding to an analysis of the water-film thickness on a clay surface, a satisfactory model for the clay mass as a whole is necessary.

The simplest type of model is one in which the clay mass is envisaged as a porous medium; in between the pores we have a clay matrix in which the clay particles are oriented on a micro-scale. From microscopic evidence, these regions of oriented clay are of the order of one micron diameter and are randomly placed with respect to one another throughout the matrix. Each of these regions is thought of as a domain.

When such a clay mass swells without external constraint, the increase in volume arises from additional water held by the clay surfaces together with an increased pore volume caused by the expansion of the clay matrix. This increase in pore volume is regarded as being proportional to the overall volume change.

For a Ca^{2+} montmorillonite, with a total surface area of 760 m.²/gm. of which 112 m.²/gm. is the external surface of the clay crystals as measured by nitrogen adsorption, the uptake of distilled water at a hydrostatic suction of 0·01 atm. was 0·91 c.c./gm. (about 1·6 c.c./gm. was obtained by Warkentin *et al.*[3]). The volume of the oven-dry clay and the oven-dry porosity of the clay mass were measured as 0·39 c.c./gm. and 0·13 c.c./gm. respectively. Assuming that the pore volume increases proportionally to the total volume of the clay mass, the swollen porosity becomes 0·33 c.c./gm. Hence, the water content associated with the clay surfaces is 0·58 c.c./gm. A $d(001)$ of 19 A. indicates a film thickness of 4·5 A. and for an internal surface of 648 m.²/gm. this film thickness corresponds to 0·29 c.c./gm. of intracrystalline water. Thus 0·29 c.c./gm. of water are associated with the external surfaces and correspond to a film thickness of 26 A. Similar calculation using a Ca^{2+} illite clay (County Grundy, Illinois) where no intracrystalline swelling is involved gives a value of 36 A. for the water film thickness on the illite surface. These film thicknesses could probably be 5–10 A. greater, since an appreciable proportion of the porosity measured in the dry state arises from incomplete contact of crystal cleavage faces, thus giving rise to an over-correction for swollen porosity.

The magnitude of these film thicknesses clearly indicates that the diffuse double layer concepts[7,8] are not applicable to the swelling of clay systems saturated with calcium ions. Furthermore, the reduction in swelling with increasing electrolyte concentration is considerably less than would be expected from diffuse double layer concepts. This is particularly noticeable for the Ca^{2+} illite, where swelling is not reduced until concentrations in excess of M calcium chloride are used. Calculations reveal that the London–van der Waals forces are not sufficient to explain the attraction between clay crystals at separations of this order and it appears likely that further development of the ideas of electrostatic attraction proposed by MacEwan[9,10] are necessary to explain the attractive forces in Ca^{2+} clay systems.

The ideas of pore swelling and the organization of a clay on a domain basis have important implications with respect to the soil mechanics concept of soil strength and soil–water hysteresis other than the final reproducible hysteresis loop. As a clay–water system dries from a situation approaching the gel state, the formation of domains of oriented crystals and the subsequent re-orientation of these domains to positions of minimum potential energy cause the actual pore volume of the mass to decrease continually. On rewetting from positions on the normal consolidation curve with different basic pore volumes the domains retain their entity and swell as such, causing the pore volume to swell proportionately to the overall volume of the clay mass and giving rise to a series of hysteresis loops. This also enables the same water content (voids ratio) to be obtained with quite different structural arrangements within the clay mass and must of necessity result in appreciable differences in the strength of the soil structure depending on the ratio of the water held in pores to that held within the domains. It is suggested that the concepts of domains and pore swelling obviate the necessity of latent interparticle forces as postulated by Parry[11].

The form of the hysteresis loops can be explained on the basis of Everett and Whitton's[12] domain theory of hysteresis.

The idea of domains as proposed here leads to a much better appreciation of the role of organic matter in bringing about stable aggregation in agricultural soils[13,14]. The polymeric molecules in soil organic matter are thought to exist as binding between adjacent domains.

The detailed presentation of the work discussed here will be published shortly.

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CHEMISTRY

Nylon Capillary Columns for use in Gas-Liquid Chromatography

The use of long, coated capillaries in gas-liquid partition chromatography was first suggested by A. J. P. Martin[1] and was developed by M. J. E. Golay[2]. Compared with the conventional packed columns, coated capillaries have provided a means of obtaining very high efficiencies with comparatively small retention times. Results that have so far been published[3] have been obtained from capillaries constructed from metal or glass (Desty, D. H., unpublished work).

The characteristics of a material suitable for constructing capillaries for gas-liquid partition chromatography are as follows: (1) the substance should show little or no adsorption to either the liquid phase or the solutes to be separated; (2) the surface of the material should be 'wettable' by the liquid phase; (3) the material should have a practical range of operating temperature; (4) the material should be capable of being drawn into capillaries of narrow diameter and even bore, with a smooth internal surface; (5) the material must have sufficient mechanical strength for the apparatus to be robust.

Nylon has these necessary characteristics if the capillaries are to be used in the separation of hydrocarbons. Nylon capillaries 0·01 in., 0·02 in. and 0·1 in. in diameter and 100 ft. long were investigated for use in the gas-liquid chromatographic analysis of aliphatic and aromatic hydrocarbons. At 23° C. these columns were found to show no adsorption effects with paraffins, and little or no adsorption effects with aromatic hydrocarbons. Benzene and toluene were eluted from an empty column with the 'air-peak', *p*-xylene showed slight retention, while cumene (boiling point 152° C.) showed more distinct retention. A maximum efficiency of 5,000–6,000 theoretical plates was obtained from the 0·1 in. diameter column, whereas the 0·01 in. and the 0·02 in. diameter columns both gave maximum efficiencies of 50,000 plates. The efficiency of these columns, however, decreased with retention time. The exact cause of this decrease has not yet been ascertained, but results suggest that it is due to a form of overloading.

From the results obtained from the 100-ft. columns, it became apparent that a column 1,000 ft. in length

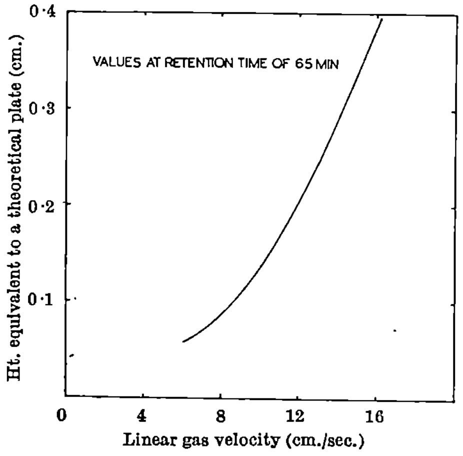

Fig. 1. Graph of height equivalent of a theoretical plate against linear gas velocity for 1,000-ft. nylon column

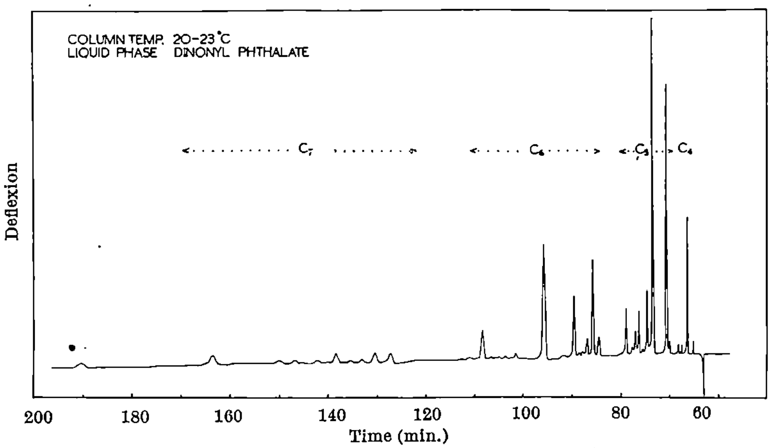

Fig. 2. Chromatogram of petroleum fraction (boiling up to 100° C.) from 1,000-ft. nylon column

should give an efficiency of between $\frac{1}{2}$- and 1-million plates. To reduce the pressure differential across the column, the 0·02 in. diameter capillary was chosen, and 1,000 ft. was coated with dinonyl phthalate by passing a 10 per cent w/v solution of dinonyl phthalate in ether through the column. At a room temperature of 20–23° C., this column was found to give a maximum efficiency of three-quarter million plates for butane, which was eluted in about 60 min. This efficiency fell to about half-million plates for *n*-hexane, which was eluted in about 90 min., and finally to 250,000 plates for *n*-heptane, which was eluted in about 170 min. A curve relating the height equivalent of a theoretical plate for this column to gas velocity is shown in Fig. 1, and a chromatogram for a petroleum fraction boiling up to 100° C. is shown in Fig. 2. The micro-argon detector was used with this column and the apparatus was found to function satisfactorily up to 100° C. A type of nylon is available, however, that is stable up to 180° C. Results have indicated that the column is slightly porous to water vapour. This can be reduced by previously coating the inside of the column with an inert 'epoxy' resin.

Full details of the work will be published later.

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Analysis by Gas Chromatography of a 'Pure' Sample with an 'Impure' Carrier

A recent analysis problem involved the measurement of trace components in a 'pure' gas stream. It was decided to attempt to analyse the stream by gas chromatography. However, no gases more pure than the plant stream were available commercially, and laboratory attempts to produce a plant stream of even higher purity on a continuous scale were not satisfactory.

It was then argued that if a gas stream of known purity were used as the carrier, 'negative peaks' were possible when deficiencies of components occurred in the sample compared with the carrier.

In theory this seemed possible, if it was assumed that impurities in the carrier gas sample formed an equilibrium down the column. On injection, the replacement of a volume of carrier gas by an equal volume of gas containing the same impurities in a lower concentration would disturb the equilibrium. Furthermore, these disturbances in any one component would travel down the column in the same manner as would a higher concentration.

In order to verify this experimentally, argon was used as the gas under investigation; it contained nitrogen, oxygen, hydrogen and methane in the 0–50 p.p.m. range as impurities. Separation was achieved using an 18-ft. column of Linde's molecular sieve No. 5 *A* with a flow-rate of 2 l./hr. Detection was by means of my design of gas discharge cells. Mixtures of the impurities were made up in argon and carefully analysed by a mass spectrometer, which served as a check on the initial mixing calculations. Choosing the mixture with an intermediate concentration of impurities as the carrier, and the low and high concentrations alternately as the sample, series of negative and positive peaks were obtained for which the calibrations were approximately the same.

Thus, the chromatographic analysis was proved possible of a gas containing impurities using a carrier gas with the same impurities in a higher concentration. For a practical application it was found possible to use a cylinder of plant gas, analysed by mass spectrometer, as the carrier gas; when the plant stream was analysed, its deficiency or excess of any component when compared with the carrier was recorded as a negative or positive peak.

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Micro Determination of Calcium

I am grateful to Dr. G. J. van Kolmeschate, of the Analytical Institute, Delft, and to Drs. H. A. Flaschka and A. J. Barnard, jun., of the Georgia Institute of Technology, and the Baker Chemical Co., New Jersey, respectively, for directing my attention to the fact that the indicator used by me[1] for the micro-determination of calcium is Eriochrome Black *T*, and therefore well known in this connexion. For this I express my regret: the error was due in part to discrepancies in the literature. However, although the use of this indicator is evidently not novel, my results show that it is possible to use it at *p*H 12–13, where other workers have found it unsatisfactory; I have therefore found it possible to determine calcium directly in the presence of magnesium. Possibly my ability to obtain a satisfactory end-point is due partly to carrying out the titration in essentially a thin film, and partly to using a high concentration of indicator—5λ of a 0·4 per cent methanol solution, or about 40 times the concentration used by Hildebrand and Reilly with 'Calcon'[2]. In this respect I find Eriochrome Black *T* to be superior to the latter indicator at such micro-levels. With the very small volumes involved, the coloration of 'Calcon' is undetectable at the recommended concentration: and using this indicator sufficiently concentrated to produce a visible coloration leads to gross inaccuracies which the use of blank determinations cannot correct at the calcium-levels it is desired to estimate. On the other hand, the high concentration of Eriochrome Black *T* required to give a detectable colour apparently does not affect the accuracy of the results.

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Lowest Oxidation States of Technetium and Rhenium

The polarographic reduction of perrhenate ion, ReO_4^-, to rhenide ion has been studied in some detail[1,2]; although the possibility of a −I state for technetium has been mentioned[3], no experimental evidence for such a state appears in the literature.

The polarographic reductions of potassium perrhenate and pertechnate in 2 *N* potassium chloride have been compared. For perrhenate, Lingane[1] found that the reduction wave was considerably larger than that expected for an eight-electron reduction to Re(−I), although he found that the *n* values tended towards this value with increasing concentration. Our results agree with Lingane's in dilute solutions, but at concentrations greater than 0·5 m*M* the reduction wave corresponds exactly to an 8-electron reduction.

For potassium pertechnate in 2 *N* potassium chloride, an 8-electron, irreversible, diffusion-controlled reduction very much the same as for perrhenate is observed, clearly showing that reduction to a −I oxidation state occurs. In dilute solutions, technetium shows a similar effect to rhenium in that the *n* values become greater than 8, although this does not occur until concentrations in the range of about 0·025 m*M* are reached. The half-wave potential of the single wave varies slightly with concentration, being −1·15 V. at 0·1 m*M* and −1·12 V. at 0·01 m*M*. The wave is well defined and would be suitable for the determination of technetium in concentrations down to 1 p.p.m.

The nature of the reduced rhenium species has generally been considered to be Re^- or $[Re(H_2O)_4]^-$, and solid rhenides have been isolated[4,5]. However, we have found that aqueous solutions of perrhenate reduced by sodium amalgam show a well-defined proton resonance in the high-field region characteristic[6] of transition metal to hydrogen bonds at ~850 cycles/sec. vs. water at 56·45 Mc./sec.; aqueous solutions of a solid rhenide after passing through a cation resin column have also been found (Ginsberg, A. P., and Miller, J. M., Columbia University, New York, personal communication) to give a similar resonance line.

In alkaline solution, therefore, the reduced 'rhenide' species contains an Re—H bond; this finding also shows that the presence of strong field ligands such as carbon monoxide, substituted phosphines, or cyanide, which are also bound to the metal atom in all previously known transition-metal complex hydrides, is not a pre-requisite for the formation of a transition metal-hydrogen bond in a complex compound.

While the precise nature of the anionic species is not known, if we accept the analytical data of Floss and Grosse[5] for the solid rhenides, namely, $Li[Re(H_2O)_4]$, then it seems reasonable to assume that the species are of the type $[HRe(OH)(H_2O)_3]^-$, $[H_3Re(OH)_3(H_2O)]^-$, etc.

Technetium may prove to form similar species. Details of this work will be published elsewhere.

We are indebted to the U.K. Atomic Energy Authority (R. C.) and the Department of Scientific and Industrial Research (W. P. G.) for maintenance grants, and to the Atomic Energy Authority and Johnson, Matthey and Co., Ltd., for the loan of technetium and rhenium, respectively.

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Effects of Electron Bombardment upon Bromides of Cadmium and Silver

Some interesting effects of electron bombardment upon certain inorganic substances were reported by de Souza Santos[1]. I have also observed rather similar phenomena with silver bromide and cadmium bromide under the electron microscope, although the type of reaction is not the same as that in de Souza Santos's experiments.

Electron bombardment of silver bromide causes local reduction to metallic silver and the reduced silver tends to gather locally[2].

In addition, cadmium bromide is photosensitive[3]. Electron bombardment reduced it to metallic cadmium[4]; the reduced metal consists of very minute crystals and keeps closely to the original form of the cadmium bromide[5]. In my experiments special care was taken that the specimen of cadmium bromide was not in contact with the film supporter in the electron-microscope or diffraction apparatus, but was held in space by a wire mesh.

Thus different metals reduced by electron bombardment behave differently, an effect that I am inclined to attribute to differences of crystal structure. Silver bromide crystallizes in the rock-salt structure, whereas cadmium bromide possesses a hexagonal layer structure which is anisotropic[6]. Fig. 1 shows the reductive process due to electron bombardment in the (001)-plane of cadmium bromide, where the formation of triangular and hexagonal holes occurs. These suggest the existence of an effect of crystal structure on the morphological changes produced by electron bombardment. The anisotropy of the crystal

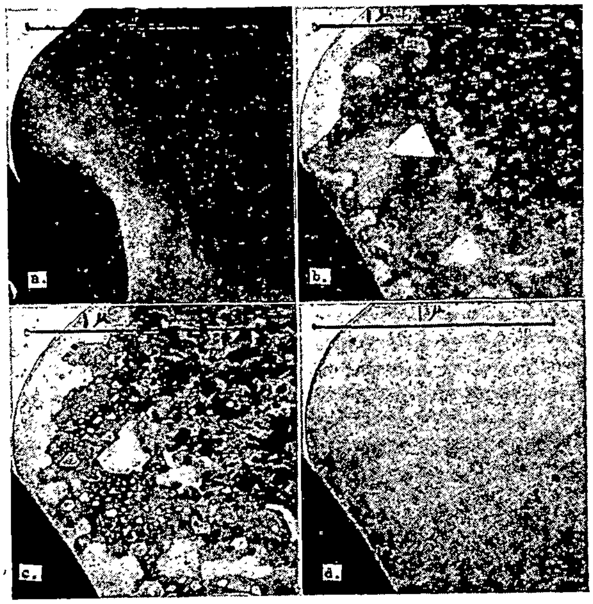

Fig. 1. Electron micrographs of same portion of (011)-plane of cadmium bromide crystal. (*a*) Before electron bombardment; (*b*) formation of triangular holes followed later (*c*) by hexagonal holes; (*d*) specimen becomes transparent to electrons. (× 3,200)

structure of cadmium bromide apparently controls the mobility of the reduced metal, so that the initial structure persists even after reduction of the original salt.

The morphological questions raised by de Souza Santos's electron bombardment experiments should be considered in the context of the crystal structure of the specimens.

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PHYSICAL SCIENCES

Advance Detonation in a Tubular Charge of Explosive

A GENERAL study of the effects of a void within an unconfined solid explosive on its detonative properties was made in these laboratories in 1941 and later; some new observations were made. One effect, as shown by rotating-mirror camera records, is that the velocity of detonation of a tubular charge is higher than normal; for example, with a cylindrical charge of cast 40 : 60-tetryl/T.N.T. (density 1·62), 1¼ in. in external diameter, with an open axial cavity, 14 in. long and ¼ in. in diameter, the steady velocity of detonation in the tube wall is 7,410 m./sec., as compared with the normal rate of 7,125 m./sec. in a solid cylinder of the same diameter[1]. Inside the cavity in these conditions a luminous phenomenon (recorded by the camera because of the translucency of the explosive) travels at a sensibly constant speed of about 12,500 m./sec., and thus out-distances the detonation wave in the wall. In the open, beyond the end of the tube, the effect is recorded as an intense flame having temporarily a still higher speed.

The results of further experiments with tubular charges are now also briefly reported; in many of them I was associated with W. B. Cybulski, (the late) W. Payman and H. Titman. First, the effects described above were frequently observed and found to vary in magnitude with the dimensions of the charge and cavity and with the nature and physical condition of the explosive. As an example of the order of the effect with a low-density charge, when fine tetryl crystals are lightly compacted (density 0·93) as a tube formed between two sleeves of 'Cellophane' ¼ in. and 1¼ in. in diameter, the velocity of detonation in the tube wall is greater than the velocity in a solid cylinder by 47 per cent; the respective values are 7,870 and 5,370 m./sec.

Secondly, the result of closing the further end of the cavity with explosive was examined. If the tube and the blocking pellet are of an adequately sensitive explosive (for example, the above tetryl/T.N.T. mixture) the result shown in the photograph in Fig. 1 may be given (film writing-speed 352 m./sec.). Three detonation waves, indicated as *A*, *B* and *C* in the diagram, can be distinguished in addition to the luminous cavity wave. The latter again precedes the annular detonation wave *A* travelling in the tube wall, and its impact with the blocking pellet is followed by the initiation of the two detonation waves *B* and *C*; the former travels on through the final pellet and the latter in the reverse direction

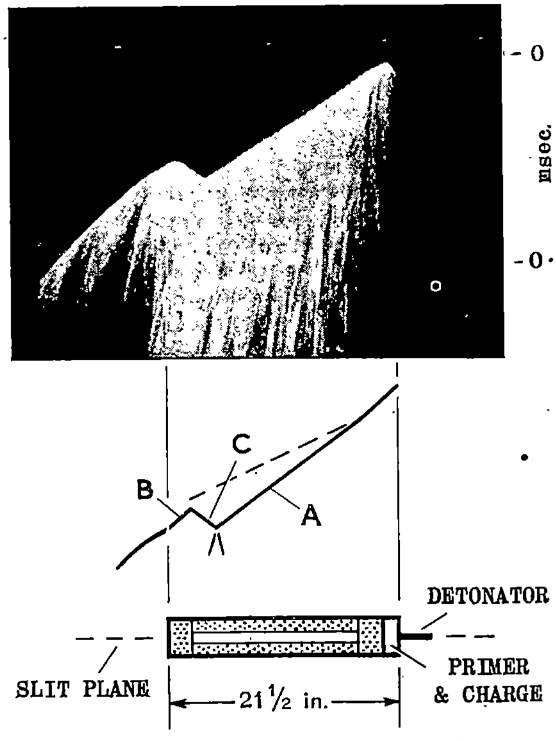

Fig. 1. Charge with single cavity and end initiation
(*Crown copyright, S.M.R.E.*)

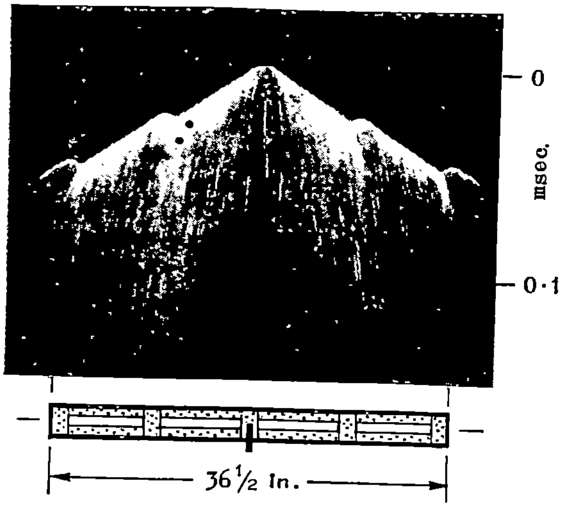

Fig. 2. Multiple-cavity charge with central initiation (*Crown copyright, S.M.R.E.*)

through the tube wall towards the oncoming wave *A*. The eventual collision of waves *A* and *C* is accompanied by a sharp increase in the brightness of the flames. The brief time-interval that elapses between the arrival of the internal wave at the end of the cavity and the first appearance of a detonation wave in the end pellet does not necessarily represent a delay in initiation; it is no more than the time that would be required for the detonation to spread spherically from a region of inception near the axis to the surface.

This phenomenon can be called 'advance detonation'. It occurs with a variety of explosives, including tetryl and gelignite, but not with those of comparatively low sensitivities nor in thin-walled tubes. Indeed, with T.N.T. of coarse crystal structure and cast without additive, not only is advance detonation absent, but also the oncoming detonation wave *A* is extinguished at the end of the cavity and all flame disappears; furthermore, wave *A* may fade before reaching that point. Border-line effects, such as an advance detonation that is delayed or proceeds in one direction only, are given by explosives of intermediate sensitivity, for example, cast tetryl/T.N.T. mixtures containing less than 30 per cent of tetryl.

Similarly, intermediate effects are given even with tetryl in charges having long or narrow cavities; in these conditions the cavity wave begins to lose speed. The attenuation is evidence of a drain of energy to the wall of the cavity, a result that is doubtless related to the enhanced velocity of detonation in the tube wall (wave *A*). The occurrence of detonation in the wall of a tubular charge with an open end, as the result of the above loss of energy, can be observed only in special circumstances, for example, with explosives at a low packing density (and therefore in a very sensitive condition) and when wave *A* has been extinguished by an annulus of inert material that has been interposed as part of the tube. Advance detonation in the wall sometimes occurs in these conditions after a comparatively long delay.

The conditions in the cavity resemble those in which advance ignition has been observed in detonating gas mixtures contained in cylindrical tubes when a shock wave, travelling ahead of the flame front, reaches the closed end of the tube; the collision of the wave with an obstruction may result either in the inflammation of the gas mixture[2] or in its immediate detonation[3]. It is concluded that the cavity wave is the sole cause of advance detonation in a solid explosive, and that at the surface of the blocking pellet struck by the wave there is a rapid and substantial transformation of energy following the impact. The cavity wave must also be the cause of the enhanced velocity of the detonation in the tube wall, possibly through the pre-compression of all or some of the material of the wall.

Some conclusions of practical importance can be drawn from these experiments. With an insensitive explosive such as T.N.T., cavitation is shown to be undesirable; it must represent in any event a loss of explosive power, but there may be a further more serious loss because of a complete failure of part of the charge to detonate. With the advance detonation that occurs with more sensitive explosives, however, some control of explosive action is afforded by cavitation, although again a net loss in total power can be expected. The detonation of a tubular charge is completed in a shorter time than that of a similar solid charge, thus leading to enhanced explosive action or greater brisance; from a knowledge of the velocities of the various waves, the length of the cavity can be chosen to give a minimum total detonation time. Further, the ring of collision of waves *A* and *C* can be regarded as a focus of brisance; multiple cavities in cascade can be used to produce a succession of such localities where desired.

These secondary results of advance detonation are illustrated in Fig. 2, which records the detonation of a suspended charge of pressed tetryl (density 1·45), ⅞ in. in diameter, and containing four separate axial cavities each 8 in. long and ¼ in. in diameter; the velocity of detonation in the walls of the hollow portions is 7,780 m./sec., as compared with the corresponding velocity in a solid cylinder of 6,875 m./sec. Owing to the opacity of the tetryl the cavity wave was not recorded, but the four points of collision in the tube surface are seen. The arched trace shows that the time of detonation is further shortened substantially by initiating the charge centrally instead of at the end. In this instance the total reduction of time is 65 per cent.

It is hoped to publish the quantitative results of this work in due course.

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[1] Woodhead, *Nature*, **160**, 644 (1947).
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Gelatin as a Photo-elastic Material

In recent investigations of contact stresses in the Charles Kolling Photo-elasticity Laboratory of this University, a clear gelatin specially supplied by local manufacturers was used for the models. Gelatin was selected in view of its low Young's modulus and its high relative stress–optical coefficient, despite its serious disadvantages discussed herein.

It was found that most of the difficulties of preparing homogeneous gelatin–glycerin models may be overcome if the precautions of Farquharson and Hennes[1] are carefully observed. Their suggested pouring temperature of 40° C. may be exceeded slightly without impairing the photo-elastic properties of the models.

The problem of satisfactory storage of gelatin models was systematically investigated with the following general results:

(1) *Storage in moist air.* Models containing 20 per cent gelatin and 12–14 per cent glycerin stored at room temperature in air of 100 per cent relative humidity remained reasonably stable in respect of water content, Young's modulus and stress–optical coefficient over a period of 200 hr.

(2) *Storage in dry ambient air.* Models containing 20 per cent gelatin and greater than 14 per cent glycerin stored on the bench, with a sheet of glass on each side of the model, were found to be reasonably stable for 200 hr. To prevent adhesion of the model to the glass, liquid paraffin (B.P.) was found to be an excellent lubricant.

(3) *Storage in a glass mould.* The storage of a model by carefully replacing it in its mould, using liquid paraffin as the lubricant, proved to be the most satisfactory method.

The time–edge effect[2] developed to a marked extent in all the models, and appeared to be unavoidable regardless of the method of storage. It may be overcome by cutting a thin layer from each loaded edge before each test. A very sharp blade must be used to achieve a smooth new edge.

Another problem with gelatin photo-elastic models is the rapid growth of bacteria in the gelatin, which seriously affects the contrast of the fringe patterns. To prevent the growth of bacteria it is recommended that, when preparing the models, 0·1–0·2 per cent (by weight) of sodium pentachlorphenate be added to the water before the gelatin is added.

Determination of the stress–optical coefficients with yellow sodium light (5893 A.), using a concentrated point load, yielded values in the range $2 \cdot 4 \times 10^4$ to $3 \cdot 2 \times 10^4$ brewsters for 20 per cent gelatin/12 per cent glycerin models, and $3 \cdot 4 \times 10^4$ to $4 \cdot 0 \times 10^4$ brewsters for 20 per cent gelatin/14 per cent glycerin models. These values are not altered by the presence of sodium pentachlorphenate. They appear to be appreciably greater than previously published values[3-5].

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Interpretation of Resonance Energies in the Photoproduction and Scattering of Pions from Hydrogen

SEVERAL maxima are well established now in the scattering and photoproduction of pions from hydrogen[1-6]. These maxima are generally considered to be due to the excitation of the proton to 'isobaric' states.

In all cases, however, the excitation energy amounts to several hundred MeV. It is, thus, of the same order of magnitude as the meson rest energies or their differences.

In this communication an attempt is made to give a numerical interpretation of the observed excitation energies.

Recently[7] it was shown that the masses of a series of heavy fermions can be described by the relation:

$$Mc^2 = 38 \cdot 46[l(l + 1) + s(s + 1)]\text{MeV}. \qquad (1)$$

Table 1. PARTICLE REST ENERGIES IN MEV.

s		Values of *l*					
		1	2	3	4	5	6
1/2	calc.	106	260	490	798	1,182	1,644
	obs.	106	266	494	792	1,189	1,645
		μ	ζ	(K)		Σ	
3/2	calc.		375	606	910	1,298	1,760
	obs.		377	603	(938)	1,311	1,760
					(P)	Ξ	
5/2	calc.			798	1,106	1,490	
	obs.			792	1,115	1,508	
					Λ		
7/2	calc.				1,375		
	obs.				1,380		

The quantum numbers *l* and *s* are taken to represent angular momentum and intrinsic spin of extended particles.

In Table 1 calculated values are given for heavy fermions, for which comparable empirical evidence exists[8-11]. The calculated and the empirical values agree in most cases within less than 1 per cent. The deviations, if not within the experimental error, may be due to electromagnetic effects or a small quadrupole correction.

One of the most interesting features of the level scheme provided by equation (1) is the occurrence of a degeneracy of the value $E = 798$ MeV. for $l = 3$; $s = 5/2$ and for $l = 4$; $s = 1/2$. Moreover, it coincides with the difference of the rest energies of a proton and of a pion (938–140) MeV. The difference in the stability of a proton and of mesons and hyperons can thus be understood as due to the possibility of resonance in the binding of a pion to a core particle with rest energy 798 MeV.

Equation (1) can be used to explain some of the resonance energies observed in pion scattering and in the photoproduction of pions from hydrogen.

The core particle ($l = 3$; $s = 5/2$) with energy $E = 798$ MeV. can be excited to form a particle with $l = 3$; $s = 7/2$; $E = 1{,}068$ MeV. The excitation energy amounts to $E = 270$ MeV. The first maximum is found for $E = 263$ MeV. (c.m.) for charged pions produced with γ-rays of 300 MeV. (lab.)[1]. This energy can be considered to represent resonance energy in the dispersion relation for nuclear reactions[12].

The excitation of the same core particle to a particle with $l = 4$, $s = 5/2$; $E = 1{,}106$ MeV. would need an excitation energy of $E = 308$ MeV. A resonance energy in scattering of charged pions was found at 299 MeV. (c.m.). (This value represents the sum of 159 MeV. kinetic energy and 140 MeV. rest energy of the meson[2].)

The superposition of these two excitations, namely, the excitation of the core particle to a particle with $l = 4$; $s = 7/2$ would require $E = 577$ MeV. A resonance energy for neutral photopions occurs at $E = 574$ (c.m.). (750 MeV. γ-rays, lab.)[3]. A maximum at this value is reported also for π^--scattering[4].

The excitation of the core particle to a particle with $l = 3$; $s = 9/2$; $E = 1{,}414$ MeV. would require an energy $E = 616$ MeV. (M2), and $E = 615$ MeV. was found recently for a maximum in the π^--scattering by hydrogen[5].

The first four excitation energies to be expected for the core particle of 798 MeV. thus agree with four of the observed resonance energies.

The existence of resonance-levels need not be due to the excitation of the core particle only, but may be caused also by the energy absorbed for pair creation.

In fact, the first calculated resonance energy $E = 270$ MeV. coincides with the rest energy of a pair of neutral pions. Their formation provides thus an alternative interpretation or a competing process for the observed $E = 263$ MeV. (c.m.) or 300 MeV. (lab.) γ-ray resonance energy for photoproduced charged pions mentioned above.

The resonance energy for photoproduced neutral pions amounts to 320 MeV. γ-ray energy (lab.) or $E = 279$ MeV. (c.m.)[4] and $E = 279$ MeV. is exactly the rest energy of a pair of charged pions. A maximum in this energy region seems to exist also for π^+-scattering[6].

The resonance energy due to the creation of a pair of particles with $l = 2$; $s = 1/2$ would be $E = 520$ MeV. A resonance energy of $E = 543$ MeV. (c.m.) or 700 MeV. (lab.) was observed with γ-rays producing positive pions[1].

The formation of a pair of particles with $l = 2$; $s = 5/2$ would require $E = 750$ MeV., and $E = 775 \pm 40$ MeV. is reported for a maximum of scattering of negative pions[5].

Table 2 gives a survey of the calculated and observed resonance energies E_r.

Table 2. RESONANCE ENERGIES (MEV.) FOR PHOTOPIONS AND FOR PION SCATTERING FROM HYDROGEN

^{2s+1}L	^6F	^8F			^6G		^8G	^{10}F	
Mc^2	798	1,068			1,106		1,375	1,414	
(Pairs)			$2\pi^0$	$2\pi^\pm$		$2^3D^\pm$			$2^4D^\pm$
E_r calc.		270	270	279	308	520	577	616	750
E_r obs. (c.m.)		263		279	299	543	574	615	775 +40
Obs. γ-rays (lab.)		300		320		700	750		
producing		$\pi^\pm$		π^0		π^+	π^0		
Scattering of		π^+			$\pi^\pm$		π^-	π^-	π^-

The rest energy $E = 211$ MeV. of a pair of muons should lead to a maximum for pion scattering at $E = 85$ MeV. pion kinetic energy (lab.), or to $E = 235$ MeV. (lab.) for the energy of γ-rays producing pions. Anomalies in these energy regions seem to have been observed[8]. They deserve thus further investigation. The resonance line need not be narrow, since the stimulated decay during a reaction appears to be much faster than the spontaneous decay.

At any rate, all resonance energies calculated for the energy-range of the observed maxima agree with the empirical values within the experimental error, in several cases with remarkable precision.

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May 1.

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'Ring Angels' over South-East England

IN the course of observations on radar 'angels' which we have been making during the past two years, we have occasionally noted formations of angels which are clearly related to the ring angels reported by Elder[1] at Ypsilanti (U.S.A.) in 1957. Fig. 1 shows a typical and fully developed ring angel which was observed on February 17, 1959. This record was obtained with a high-power L-band radar of conventional design; the signals were displayed on an ordinary plan position indicator with video map superimposed on the radar signals. The antenna was rotated at four revolutions per minute and the displays were photographed on each scan. If a film secured in this way is exhibited through an ordinary ciné projector running at sixteen frames per second, an acceleration of 240 times is obtained, and in these circumstances the dynamic growth of the ring angel can be clearly observed. The ring angel commences as a strong point echo; it then extends into an annular ring, to be followed by other rings at approximately equal intervals of time. The whole phenomenon has precisely the same appearance as the ripples on a pond expanding from a point of disturbance. In the case of the rings shown on Fig. 1, eighteen rings were emitted from the centre with an average periodicity of 2½ min. and a maximum diameter of 20 miles was achieved.

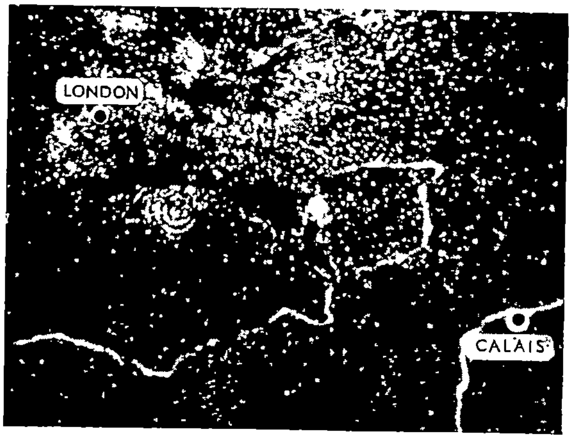

Fig. 1. Ring angel of February 17, 1959

In the course of the present work we have observed sixteen such incidents, and the geographical distribution of the active centres is shown on Fig. 2. The ring angels tend to occur around certain active regions which have been marked upon the map as small circles. The ring located at Ipswich has yielded five incidents during the past four months. Detailed examination of the map and of the areas involved has not revealed any topographical feature which might be a contributory factor to ring formation; nor are they regions of unusual bird-roosting.

It will be noted that no ring angels have been observed over the sea, and that the ranges of the rings from the radar station, when taken in association with the radiation pattern of the radar, suggest that the reflecting or scattering elements of the ring occur at a low altitude only. It has been possible to make some height measurements with the aid of a 10-cm. nodding height-finder radar. These results,

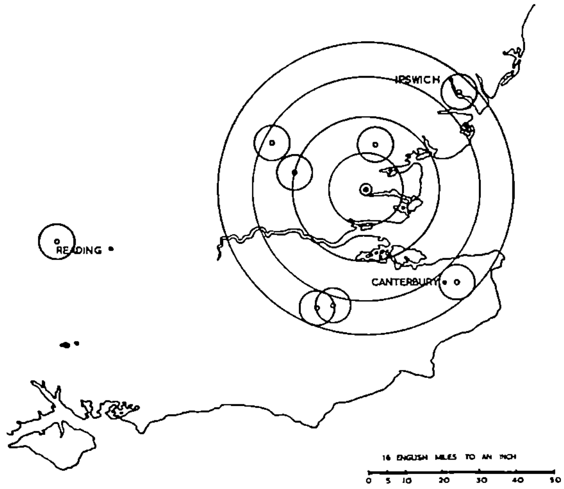

Fig. 2. Location of ring angel centres

if interpreted as heights in the ordinary manner, indicate that the altitude of the rings does not exceed 2,000 ft.

These rings show many points of similarity with those reported by Elder, but there are certain important differences, the chief of which is the time of occurrence. The rings we have observed have all occurred at the sunrise period, and in most cases the presence of the ring centres has been noted for a few minutes before sunrise. This correlation with sunrise is quite vividly seen on the radar display, since the sun shows itself as a radial noise point upon the plan position indicator and ring angels and solar noise then exist simultaneously upon the tube. We have noted as many as three incidents occurring simultaneously about the various active centres. It will not be possible to see the form of the annual variation until a year's cycle is completed in September 1959, but from our records to date there appears to be a tendency for the rings to be more prevalent during the winter months.

The rings have been observed during a variety of weather states, including widespread fog, but the ground wind-speed on all occasions has been less than 15 knots. The approximate circularity of the rings can be assessed from Fig. 1 and there has been only one formation which has shown some distortion of a form that is correlated with the wind direction; in no case has there been definitely measurable displacement of the centre of the disturbance.

Measurements on ring velocity and periodicity have been made from the film records, but no great accuracy can be claimed for the results, due to the diffuse nature of the phenomenon. The periodicity or interval between successive rings has varied from 1½ min. to 12 min. for the different active centres, while the interval has changed by as much as 50 per cent during the course of one incident, for example, from 2 min. to 3 min. The range of velocity of expansion for all the incidents so far observed is 25–55 m.p.h. In the case of the most perfect ring formation, good measurements were possible upon the first four rings emitted and these possessed velocities of 36, 30, 21 and 22 m.p.h. respectively.

As the rings expand they become very diffuse and are seldom continuous; the maximum diameter so far achieved is 30 miles. The debris from the ring then disappears rapidly and does not continue to move outward as a number of independent bird-type angels.

On the evidence which has so far been accumulated, it is difficult to decide whether ring angels are due to meteorological causes or, alternatively, are to be attributed to bird movements such as have been shown to be the probable explanation of a high percentage of ordinary radar angels by various workers, including Harper[2] and Tedd and Lack[3]. The observations are being continued and will be reported in detail elsewhere.

We wish to thank our colleagues, Mr. P. Way and Mr. G. Downie, for assistance in making the observations, and the engineer-in-chief of Marconi's Wireless Telegraph Co., Ltd., for permission to publish this communication.

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May 8.

[1] Elder, F. C., Proc. Sixth Weather Conference, Cambridge, Mass. (1957).
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Microseisms at Scott Base

Since March 1957, a seismological station has been in operation at Scott Base (77° 51′ S., 166° 48′ E.) on Ross Island. The seismometers, three Benioff-type instruments, feed three short-period (0·2 sec.) galvanometers and three longer-period galvanometers (vertical and east–west 25 sec.; north–south 10 sec.). The installation was not explicitly designed for microseismic recording, the main objective being the determination of local seismicity. However, following some interesting qualitative observations at the Base, a preliminary examination of microseismic amplitudes and periods has been made.

In Fig. 1*a* are shown, for 1958, the weekly mean amplitudes (arbitrary units) of 6-hourly microseismic activity on the short-period component of the vertical seismometer. The microseisms are 1–4 sec. period and, as is normal, periods increase with increasing amplitudes. However, abnormally, at Scott Base the maximum amplitudes occur during the summer with microseisms virtually absent during the winter on this component. This pronounced seasonal variation must be related to the presence of ice on the surface of the Ross Sea. The ice forms during autumn and breaks up in the late spring. By mid-winter, freezing of the sea is probably complete, though due to storm and tide action this cover may be broken. During late winter the pack ice is believed to extend beyond the continental shelf, thus inhibiting surface motion of the sea over the continental region.

There is little doubt that the 1–4 sec. microseisms recorded at Scott Base are due to events within the Ross Sea, which cause microseisms whenever ice conditions permit. This is in accord with Donn[1], who states that restricted storms or cold fronts over relatively shallow continental shelf waters generate microseisms of periods of 2–4 sec. Analyses of sea and weather conditions in relation to microseismic

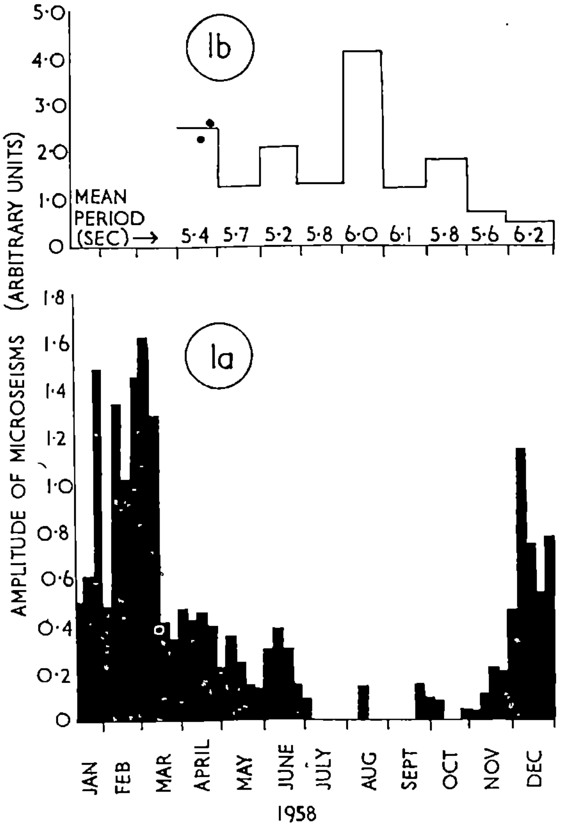

Fig. 1. (*a*) Weekly mean amplitudes of microseismic activity on short-period vertical record, Scott Base, 1958. Based on five typical groups at 00, 06, 12 and 18 hr. daily. (*b*) Monthly mean amplitudes of long-period microseismic activity on long-period north–south record, Scott Base, 1958. Based on five typical groups at 00, 06, 12 and 18 hr. G.M.T. every seventh day. Monthly mean periods are given (in seconds) at base of histogram

activity are widespread in the literature but the mechanism of generation and propagation is still unresolved and theories pertaining to it increase[2]. It may be possible to use a knowledge of the pack ice morphology (amplified by aerial photography) as a constraining factor in the examination of these theories.

Microseisms of the 4–10 sec. type appear throughout the year on the north–south component with the 10 sec. galvanometer. By taking the 6-hourly microseismic characteristics on every seventh day and computing monthly means, the histogram in Fig. 1*b* has been derived. No satisfactory values for the months of January, February and March 1958 can readily be derived for these longer-period microseisms because of interference by shorter-period activity, which follows the same seasonal pattern as that on the short period vertical record. Mean periods (in seconds) of all observations are recorded for each month.

There may be a seasonal variation of the 4–10 sec. microseisms with a minimum in the summer; the results presented are certainly insufficient to establish this. But the major point of interest is that these microseisms persist undiminished throughout the winter. Their origins probably lie in the cyclones over the oceans surrounding the antarctic continent; and it seems impossible that wave or surf action at the coast could play any part in their generation or transmission.

This communication gives a broad picture of the principal events. There are many details of interest and these will be studied extensively in the future.

Lieut. F. Faggioni, of the Italian Navy, was the seismologist at Scott Base during 1958.

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A Possible Experimental Test of Einstein's Second Postulate

As is well known, Einstein's special theory of relativity rests on two postulates: (1) the postulate of relativity; (2) the postulate of constant light velocity, which says[1] "that light is always propagated in empty space with a definite velocity c which is independent of the state of motion of the emitting body". For the first postulate there is much experimental support; for the second, none. It is not generally appreciated that the experiments often held to confirm the kinematical part of Einstein's theory are, in fact, evidence that the Maxwell–Lorentz electromagnetic equations are invariant to the Lorentz transformation, since the forces and velocities concerned are determined from those equations and not by direct measurement.

In view of difficulties which have recently arisen, it is highly desirable to test the kinematics of the theory. It is often said that an experimental test of the second postulate is impossible since the clocks used would have to be synchronized by assuming its truth, but this is not so. If beams of light were emitted from the same point at the same instant from two relatively moving bodies, the postulate could be confirmed or otherwise by observing whether they arrived at a distant point together or successively; it would not be necessary to make a precise measurement of the times of travel. The frequencies need not be the same (the Doppler effect would make this unlikely in any event) provided the effect of the intervening air on the velocities was taken into account.

It might not be beyond the power of modern techniques to make this test by a purely terrestrial experiment, in which the motion of the sources remains effectively constant during the passage of the light. Forty years ago Majorana[2] attained a velocity sufficient to test the indifference of the Michelson–Morley experiment to the velocity of the source, but this, of course, only confirmed the first postulate. My purpose here is to urge the importance of making this test if possible, in view of the very great amount of theory which at present rests on an assumption.

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[1] *Ann. Phys.*, **17**, 891 (1905); English translation in "The Principle of Relativity" (Methuen, 1923).

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FORTHCOMING EVENTS

(*Meeting marked with an asterisk * is open to the public*)

Tuesday, June 23

Society for Endocrinology (at the Royal Society, Burlington House, Piccadilly, London, W.1), at 5.30 p.m.—Prof. Charles H. Best (Toronto): "A Canadian Trail of Medical Research".*

Wednesday, June 24

Geological Society of London (at Burlington House, Piccadilly, London, W.1), at 5 p.m.—Mr. E. G. Poole and Dr. A. J. Whiteman: "The Glacial Drifts of the Southern Part of the Shropshire-Cheshire Basin and their Status in British Pleistocene Stratigraphy".

British Psychological Society, Medical Section (at the Medical Society of London, 11 Chandos Street, Cavendish Square, London, W.1), at 8.30 p.m.—Mr. L. Z. Freedman: "Research in Psychiatry and Law".

Thursday, June 25

Royal Anthropological Institute (at 21 Bedford Square, London, W.C.1), at 5.30 p.m.—Annual General Meeting. Dr. J. A. Fraser Roberts: Presidential Address.

Friday, June 26

Ciba Foundation for the Promotion of International Co-operation in Medical and Chemical Research (at the Royal Institution, 21 Albemarle Street, London, W.1), at 5 p.m.—Prof. Pasteur Vallery-Radot (Paris): "Le Rôle de l'Intuition dans la Recherche Médicale" (11th (Annual) Ciba Foundation Lecture).

APPOINTMENTS VACANT

Applications are invited for the following appointments on or before the dates mentioned:

Assistant in Mathematics—The Secretary of University Court, The University, Glasgow (June 27).

Assistant, Grade B (with a good honours degree or equivalent, together with teaching, research or industrial experience), in Chemistry at Wolverhampton and Staffordshire College of Technology, to teach inorganic chemistry to H.N.C. and G.R.I.C. Part 1 standard—Clerk to the Joint Education Committee, Education Offices, North Street, Wolverhampton (June 27).

Lecturer (able to teach inorganic, organic or physical chemistry to Special (Honours) Degree Standard) in Chemistry—The Clerk to the Governors, Woolwich Polytechnic, London, S.E.18 (June 27).

Lecturer in Chemical Pathology—The Secretary, St. Mary's Hospital Medical School (University of London), Paddington, London, W.2 (June 27).

Lecturer or Assistant Lecturer (with special interests in organic chemistry) in Chemistry—The Registrar, The University, Sheffield (June 27).

Research Fellow in Mathematics—The Secretary of University Court, The University, Glasgow (June 27).

Lecturer (Grade II) in the Department of Physics, and an Assistant Lecturer in the Department of Physics—The Registrar, The University, Bristol (June 30).

Lecturer in Physical Chemistry—Prof. R. M. Barrer, F.R.S., Chemistry Department, Imperial College of Science and Technology, London, S.W.7 (June 30).

Lecturer in the Department of Natural Philosophy, and Assistants (3) in the Department of Natural Philosophy—The Secretary, The University, Edinburgh (June 30).

Lecturer in the History of Science—The Registrar, The University, Leicester (June 30).

Psychologist (with an honours degree or equivalent qualification in psychology, and preferably postgraduate research experience in experimental or clinical psychology), to give assistance to the Senior Psychologist—The Secretary, National Hospitals for Nervous Diseases, Queen Square, London, W.C.1 (June 30).

Assistant Lecturer in the Department of Biochemistry—The Secretary, University College, Gower Street, London, W.C.1 (July 6).

Assistant Lecturer or Lecturer (with an honours degree and preferably experience in hydraulics) in the Department of Fluid Mechanics—The Registrar, The University, Liverpool (July 6).

Demonstrator (preferably with a knowledge of plant physiology or biochemistry) in the Department of Botany—The Registrar, The University, Liverpool (July 6).

Chair of Mathematics in Fourah Bay College, Sierra Leone (University of Durham)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (July 7).

Lecturer (preferably with a special interest in statistics) in Mathematics; and a Lecturer in Inorganic Chemistry at Fourah Bay College, Sierra Leone (University of Durham)—The Secretary, Inter-University Council for Higher Education Overseas, 29 Woburn Square, London, W.C.1 (July 7).

Research Assistant (veterinary surgeon or graduate in microbiology) in the Department of Veterinary Pathology, for work on the pathogenesis of fowl typhoid—The Registrar, The University, Liverpool (July 7).

Assistant Lecturer or Lecturer in Astronomy—The Secretary, University College, Gower Street, London, W.C.1 (July 13).

Biometricians (with an honours degree in mathematics and some industrial training, and preferably experience in consulting work or in the analysis of experimental results) in the Agriculture Department, Wellington, New Zealand, to assist in the section which advises on the design and undertakes the analysis of research work—The High Commissioner for New Zealand, 415 Strand, London, W.C.2, quoting Ref. No. B.11/2/15 (July 17).

Lecturer/Senior Lecturer in Applied Mathematics at the University of Sydney, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (Australia, July 25).

Foundation Chair of Philosophy in the University of New South Wales, Australia—The Agent-General for New South Wales, 56 Strand, London, W.C.2 (Australia, July 31).

Senior Lecturer in Botany at Canberra University College, Australia—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (August 1).

Assistant Experimental Officer (male graduate in agriculture or agricultural botany) in the Department of Herbage Agronomy to carry out field experiments on methods of establishing leys—The Secretary, The Grassland Research Institute, Hurley, Maidenhead, Berks.

Assistant Lecturer (with special qualifications in applied mathematics) in Mathematics—The Registrar (Room 22, O.R.B.), The University, Reading.

Chemist or Biochemist, for research in the steroid field—The Director, Group for Research on the Chemical Pathology of Steroids, Jessop Hospital for Women, Sheffield 3.

Chemist (with a good honours degree in agricultural chemistry or chemistry) in the Department of Agriculture, Uganda, for research on soil fertility problems connected with tropical crop rotations, manures and fertilizers—The Director of Recruitment, Colonial Office, London, S.W.1, quoting BCD.63/9/09.

Demonstrator in Physical Chemistry—The Registrar, The University, Nottingham.

Demonstrator or Research Fellow (preferably graduate with a knowledge of aerodynamic theory and wind tunnel experiments) in Aerodynamics—The Recorder, College of Aeronautics, Cranfield, Bletchley, Bucks.

Electron Microscopist, to study fine structural changes in cells following radiation, "g" force, stress, high frequency vibration, etc.—Chairman, Department of Anatomy, Emory University, Atlanta 22, Georgia, U.S.A.

Head of the Department of Pharmacy—The Registrar, Bradford Institute of Technology, Bradford 7.

Lecturer in Electrical Engineering at Brighton Technical College, to teach to Professional Diploma and Higher National Certificate standard—The Director of Education, 54 Old Steine, Brighton.

Lecturer in Mathematics, and a Lecturer in Statistics and Mathematics—The Registrar, Bradford Institute of Technology, Bradford 7.

Lecturers in Mathematics, Physics, Biology and Biochemistry—The President, University College, P.O. Box 399, Addis Ababa, Ethiopia.

Master (with a good honours degree) to take charge of Chemistry and to teach from IVth to VIth Forms (at least to *A*-level)—The Headmaster, St. Edmund's College, Old Hall Green, Ware, Herts.

Physicist (with at least a second-class honours degree or equivalent qualification), to work in a team engaged on the basic research on powder pressing and sintering and allied processes—The Senior Recruitment Officer, Atomic Weapons Research Establishment, Aldermaston, Berkshire, quoting Ref. 2108/34.

Reader in the Department of Electrical Engineering—The Registrar, Royal Technical College, Salford 5, Lancs.

Research Assistant (engineering and science graduate), for research into oil fuel combustion—R. P. Fraser, Department of Chemical Engineering, Imperial College of Science and Technology, London, S.W.7.

Research Fellow (physical chemist or biochemist), for work on virus substructure in conjunction with a team studying the structure of viruses by physical methods—The Secretary, Birkbeck College (University of London), Malet Street, London, W.C.1.

Senior Lecturer, and a Lecturer in the Department of Electrical Engineering—The Registrar, Royal Technical College, Salford 5, Lancs.

REPORTS and other PUBLICATIONS

(*not included in the monthly Books Supplement*)

Other Countries

Bibliographien des Deutschen Wetterdienstes. Nr. 9: Agrarmeteorologische Bibliographie, 1957. Bearbeitet von Max Schneider. Pp. x+92. (Offenbach: Deutschen Wetterdienstes, 1958.) [193

Indian Association for the Cultivation of Science. Annual Report for 1957–58. Pp. 52. (Jadavpur, Calcutta: Indian Association for the Cultivation of Science, 1959.) [193

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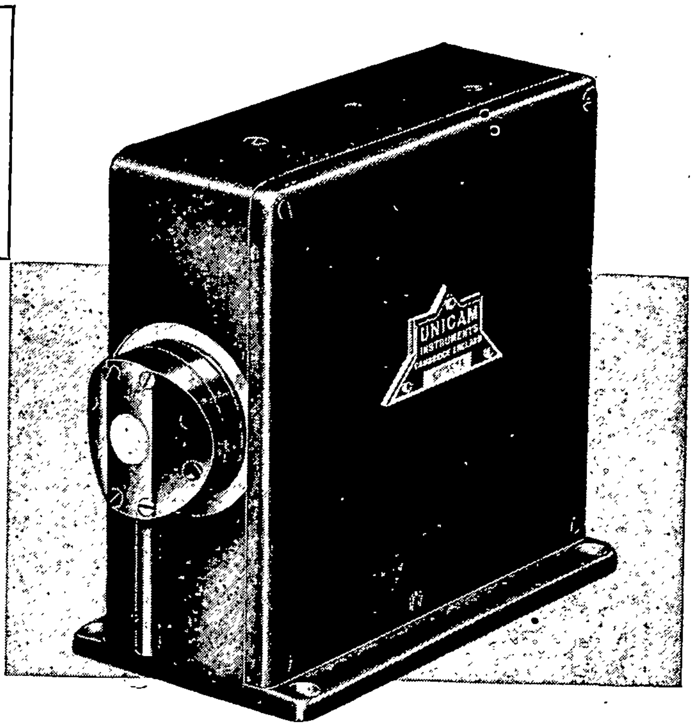

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EXPANSION OF SCIENTIFIC AND TECHNICAL EDUCATION

"ONE determinant of a nation's greatness," writes Dr. Detlev Bronk in his chairman's foreword to the eighth annual report of the U.S. National Science Foundation, "is its courage to choose between the important and the less important. A nation achieves greatness by determined devotion to the things that matter most as it sacrifices the unessential." Dr. Bronk refers particularly to forthcoming debates in the United States on expenditure on scientific teaching and research, and his words are no less applicable to continuing discussion in Britain as to expenditure on education and the balance between that expenditure and the research effort. The account of the Foundation's expanding effort in improving the quality of education in science is indeed the feature of the 1958 annual report which is of most interest to British readers. Educational structures differ widely in the two countries, but the main problems are largely similar, and experience gained in one is likely to have real value in the other, even if methods can rarely be applied without adaptation.

The background to this expansion is well outlined by Dr. A. T. Waterman in his statement as director of the Foundation. Following President Eisenhower's 'messages' of November 1957 and June 1958, particular attention was directed by the Foundation to the development of the capacity of the United States in scientific and technical research, and to its educational resources in science and engineering. Besides the increased responsibilities of the Foundation itself in the field of education, the National Defense Education Act represents a step towards improving the educational system generally ; but Dr. Waterman points out that all the measures already adopted are only a beginning. There appears to be no immediate prospect of adequate salaries for school teachers, of adequate school buildings and facilities, or of adequate facilities for recruiting sufficient competent teachers. Plans for dealing with important areas of research are still inadequate, and the urgent problem for science and engineering in the universities of the United States is to secure modern laboratories and research equipment, including rather costly equipment for the larger institutions, and to provide for larger capital research facilities to be used nationally or at regional centres. The training of more scientists also calls for extended laboratories and equipment, and maintenance and operation require expanding funds.

The problems are thus essentially the same as those with which the Advisory Council on Scientific Policy is concerned in Britain, but Dr. Waterman is not satisfied that in the United States they are faced with sufficient determination and realism. Making all allowance for the internal issues which complicate decisions, such as the relative responsibility of the Federal Government and State and local authorities for education, the clash between national policy and individual initiative and aspiration, Dr. Waterman considers that lack of realization and determination on the part of its citizens hinder scientific and educational advance in the United States. A clear conception of national objectives, how they can be achieved, and the citizen's part and responsibility in that task is a first essential, and he suggests that the Federal Government has a first responsibility to see that the problem is fully understood by the people. It must also provide direct support according to carefully devised plans and consider seriously ways and means of increasing substantially funds from other sources.

As broad objectives of national policy, Dr. Waterman puts forward the full development of individual and collective capabilities, and the identification and selection of the fields of effort which merit maximum expenditure of money and man-power. In science, the maximum emphasis should be placed upon the relatively modest needs of basic research so as to discern the possibilities of progress in technology, followed by careful choice of the fields for development that require large capital sums. Those objectives could largely be accepted as valid for Britain, though the distribution of resources and the selection of fields for development would not necessarily be similar, quite apart from any considerations of Anglo-American co-operation.

Reviewing Federal activity in the field of education, the report points out that while Congress has already increased threefold the 1959 appropriation for the Foundation's educational programme (compared with the five-fold increase recommended by the President in January 1958), the National Defense Education Act of 1958 was the first general Federal aid-to-education legislation for ninety-six years, and it re-affirmed the primary educational responsibilities of State and local communities. Apart from providing for loans to students to enable them to attend college, for awards of graduate fellowships and for State grants for vocational programmes for training technicians, under the major administrative responsibility of the Department of Health, Education and Welfare, the Act initiated a Science Information Service in the National Science Foundation to develop new and improved methods for disseminating scientific information.

Some details of the Foundation's educational activities during the year are given in the report. There are in the United States some 140,000 high-school teachers of science and mathematics, though a significant proportion are not adequately trained, and in the spring of 1958, 16,000 of them applied for admission to the summer schools which the Foundation sponsored. Of these, 6,300 teachers received support from the Foundation grants at summer schools averaging seven weeks in duration. Grants were also made to nineteen universities for similar schools in science and mathematics during the school year 1958–59, in which 925 teachers were trained, and for 1958–59 about thirty summer schools are planned. About 3,000 high-school teachers attended other 'schools' offering courses out of school hours, and for 1959–60 the number of such institutes supported by the Foundation is to be increased from 86 to about 200. The Foundation also proposes to offer about 550 fellowships for graduate teaching assistants for the summer of 1959, to enable them to pursue, full-time, their own study programmes during the summer months, and about 750 science fellowships for secondary school teachers of science and mathematics who hold bachelor's degrees to enable them to pursue a personal study programme over one to three summers.

Besides these programmes attempting to improve the qualifications of existing teachers and to shorten the time in which qualifications can be obtained, the Foundation is trying out new methods of increasing the understanding of science by young people. These are of three types. Some seek to enlist the interest in and understanding of science, mathematics and engineering by students at all levels. These include a travelling high-school science library programme, a travelling science demonstration lecture programme, particularly in such subjects as solar radiation, atomic structure, nuclear reactions and space travel (a programme which enables distinguished scientists to visit small colleges and universities for several days), a science club project and a summer training programme for secondary school students. The second type comprises a variety of teacher-training projects, and the third stresses studies of the content of science curricula in secondary schools, in which new and imaginative approaches to instruction in science have resulted from the judgment and experience of scientists and teachers, including the development of an entirely new course in physics for the high-schools.

Some of these programmes are extensions or developments of projects on which the National Science Foundation had already embarked, and parallel activities are indeed to be found in Great Britain. The Minister of Education, for example, has already recognized the need for examining our methods of teaching science and our curricula with fresh minds. The Advisory Council on Scientific Policy is known to be aware of these problems, and an important session at the Home Universities Conference last December on standards of teaching and techniques and the supervision of students in universities showed that the universities are already considering what can be done, quite apart from the implications of the forthcoming expansion. To a limited extent, the opportunities which new techniques, such as sound broadcasting and television may provide, are being explored, although there is nothing exactly parallel to a project supported by the National Science Foundation and sponsored by the American Institute of Biological Services which seeks to evaluate the effectiveness of the use of experimental colour television films in biology.

The annual report of the National Science Foundation is thus a welcome reminder of possibilities in meeting the shortage of science teachers and in expanding our output of scientists and technologists. It does more than point to possibilities which may here have been overlooked or been insufficiently examined. It sets the whole problem in its proper perspective and emphasizes the need for looking at education as a whole and for dealing with it with real determination, urgency and vision.

On that there are two points to be made. A first priority is the creation of a wide public understanding of all the issues involved; this is a task to which professional associations generally, and not those of teachers alone, should be addressing themselves. The British Association is already supporting important projects to this end, as the American Association for the Advancement of Science has done, and some of the professional organizations are already taking an increasing interest in the training of those entering their own professions. It should not be a difficult step from such work to participation in the task of developing a wider public understanding of the implications of education generally.

Secondly, while the American effort in the improvement of the quality of scientific and technical education and the expansion of its scale, vastly exceeds the present effort in Britain, it is important to remember that mere expansion itself is not enough. Expenditure on education in Britain must be appropriate to national needs and resources, and conditioned by them and by our ideals and traditions, not by those of other countries, however closely associated. Moreover, it is at least as important to see that the most effective use is made of expenditure as to see that the expenditure is adequate. As in research, there is real danger that full use will not be made of existing facilities and expenditure through failure to provide the essential equipment, aids and supporting technicians.

In this connexion, the discussion at the Home Universities Conference* is suggestive. Prof. R. J. Pumphrey challenged the validity of the existing lecture system, and he pleaded for wider use of libraries and reading and the more generous provision of such facilities; and although others, like Prof. J. T. Brindoff, did not agree that the university lecture had outlived its usefulness, there was strong support for his plea for expansion of the university library, though it was also pointed out that the student has yet to learn the art of reading in a library. It was clear enough that fresh thought is already being given to existing methods and techniques, and that a comparatively minor increase of expenditure at particular points would enhance the present efficiency of both teaching and research. Indeed, Prof. B. Bleaney showed that there is very real danger so far as physics is concerned, unless larger Treasury grants are forthcoming. It was no less apparent, however, that if in the expansion of education in Britain already proceeding the full benefits are to accrue, to the individual and to the community, there must be clear conceptions as to the exact functions of our educational institutions, the purposes they are to serve and their relations to one another. These must be in harmony and the resources placed at their disposal appropriate to the function to be served, if we are to avoid either waste of effort and resources or to achieve such a standard of education and supply of trained men and women as Britain needs to use the opportunities that confront us in this age of rapid technological change.

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* Report of the Proceedings of the 1958 Home Universities Conference convened by the Committee of Vice-Chancellors and Principals and held in the William Beveridge Hall, University of London Senate House, 12th and 13th December, 1958. Pp. 120. (London: Association of Universities of the British Commonwealth, 1959.) 5s.

JOHN DALTON

The Biographical Approach to John Dalton

By Frank Greenaway. *Memoirs and Proceedings of the Manchester Literary and Philosophical Society,* Vol. 100, 1958–59. Pp. vi+98+11 plates. (Manchester: Manchester Literary and Philosophical Society, 1958.) 21*s*.

THE hundredth volume of the *Memoirs and Proceedings* of the Manchester Literary and Philosophical Society consists of a memoir by Frank Greenaway on "The Biographical Approach to John Dalton". It deals with the older biographies written by Henry, Angus Smith, Lonsdale, and Roscoe, and also gives, for the first time, a connected account of the newer work of Roscoe and Harden, Meldrum, and Gee, Coward, and Harden, as well as of some later publications.

This essay is very interesting, and a good deal of painstaking work has evidently gone into it; but it fails, in my opinion, to do justice to Dalton. It includes too much which is irrelevant and omits too much which is essential to a proper understanding of the place of Dalton in the history of chemistry. Some justification for the last statement can first be given.

It has often been said that before the enunciation of his atomic theory Dalton did little or nothing of importance. In fact, Dalton had published work on the theory of mixed gases and the state of water vapour in the atmosphere, on the conduction of heat in liquids, on the vapour pressure of water, and on the expansion of gases by heat; and if he had done nothing else he did, and would still, rank high. Mr. Greenaway says that in his early meteorological work, "Dalton slipped into a groove of study which led him to a position he never fully understood". It led him to the discoveries mentioned above and to ideas which, unless we knew that they were first published by Dalton and were initially received with incredulity, we might think are self-evident.

It has also often been said that after the publication of his atomic theory Dalton did no work of importance; he was, says Mr. Greenaway, "an anachronism". Yet some of his later work, such as that on the combustion of hydrocarbons, on the vapour density of ether, and on the isomeride of ethylene in coal gas is really important.

Another old error which is repeated is that Dalton was a coarse and inaccurate experimenter. His work on gas analysis, which (as everybody who has done any knows) is difficult, is quite exceptionally good, and although Mr. Greenaway dismisses the third volume (II, ii) of the "New System" in a word or two as of no interest, it contains some surprisingly accurate work on the equivalents of metals which has been pointed out by Trengrove. A mention of Dalton's "undeserved reputation as a chemist" is unnecessarily severe on the judgment of contemporary chemists.

Dalton's early work on the aurora is given but it is not mentioned that Faraday later proposed the same theory without naming Dalton; no reference is made to Dalton's later experiments on the composition of the higher atmosphere and his explanation of the results, quite recently proposed again as original.

Dalton did not read many books, but the suggestion that "his often-quoted claim to be independent of them may well have been an impromptu attempt to conceal a feeling of inferiority in the face of those who were more accustomed to them", is one of those random guesses which sometimes pass for biography. One of the books Dalton read in his early period is Bishop Watson's "Essays", on which F. Sherwood Taylor's over-clever statement that it could have been written in a year and "smells more of the lamp than the laboratory" is quoted. This book (in five volumes) records Watson's visits to mines and factories extending over many years, and contains some extensive research of his own which is known to physical chemists. Watson's work on gunpowder is also well known. This sort of history simply will not do.

Dalton's mentality seems to have been relatively straightforward as compared with personalities such as Newton, Priestley and Lavoisier. Mr. Greenaway gives an anecdote (p. 7) about Granville (who is otherwise little known) revisiting Dalton in old age and finding him busy trying to loosen a stuck glass stopper. Dalton gently resisted an attempt to assist and finally released the stopper himself. Then, although obviously busy, he had a few courteous words with his unrecognized visitor and got rid of him. This was typical of Dalton, but all Mr. Greenaway gets out of it is that "there was a little glow still in the grey ash of the man".

The section on the origin of Dalton's atomic theory is one of the best, but it too fails to bring out some important matters. Mr. Greenaway thinks that earlier writers have been inconsistent in saying that the origin goes back to Newton while Dalton used a theory of heat different from Newton's. A little might have been said about Newton's own use of this theory of heat, and why Dalton adopted a different one. The influence of Lavoisier's "Traité" could have been considered, and particularly how Dalton's criticism of an erroneous theory of mixed gases contained in it was related to the development of his own theory.

The final section of the essay is a rather confused assembly of some recent pronouncements on the philosophy of making discoveries; it is not easily understood.

If I were asked to hazard an opinion I would say that Dalton has been too much for many of his biographers; the most successful of these was probably Roscoe, largely because he was a chemist, had read Dalton carefully, and had a good knowledge of the state of physics and chemistry when Dalton began his work. The same qualifications are needed in a future biographer of Dalton, who will have the advantage of new knowledge which has accumulated since Roscoe wrote.

Mr. Greenaway's essay gives a good if incomplete summary of this new knowledge, and he has added a few new morsels—no mean achievement in the field, since much of the material has been lost. He deserves thanks for what he has done. J. R. PARTINGTON

APPLIED ANALYSIS IN THE U.S.S.R.

Approximate Methods of Higher Analysis

By L. V. Kantorovich and V. I. Krylov. Translated from the Russian by Curtis D. Benster. Pp. xv+681. (Groningen: P. Noordhoff, Ltd., 1958.) n.p.

THE first edition of this book appeared in 1936, as "Methods for the Approximate Solution of Partial Differential Equations"; it dealt with boundary value problems for linear equations. The title was changed to the present one for the second edition (1941), on the inclusion of an extended treatment of conformal mapping, and an account of the numerical solution of integral equations. The present translation is from the 1952 edition,, which does not differ greatly from the earlier editions: the authors promise a complete revision which shall take account of the substantial progress made since 1941, when no doubt the use of linear operators and function spaces, for example, will find a place. In the interim, a translation is most welcome, since the book as it stands is probably alone in its class, yet for linguistic reasons many of us have been debarred from immediate knowledge of its richness of content. In spite of an increasing flow of translated books and periodicals, it is not easy to acquire a full insight into the rapid growth of Soviet mathematics, though F. J. Weyl, writing from the U.S. Office of Naval Research, measures the will to do so by his remark: "It is a unique distinction of the mathematical community to have never been taken in by the myth, now generally shattered, that Russian science merely followed the lead of the West—at a respectful distance".

The book in each of its main sections exhibits the intention of pressing the processes of pure mathematics beyond the domain of form and theory to the region of numerical calculation, to numerical approximations accompanied by estimation of error. Methods are illustrated by examples from various fields of applied mathematics, carried out to detailed numerical conclusions with evaluations of bounds to errors. The first section deals with solutions of Laplace's equation by infinite series, including Fourier series, with paragraphs on methods of accelerating the convergence. The second section discusses numerical methods for solving integral equations of Fredholm's type, with some emphasis on the 1930 method of N. M. Krylov and N. N. Bogoliubov, illustrated by solving the Dirichlet problem for an elliptic boundary. In the third section, the method of nets, which replaces a partial differential equation by a set of finite difference equations, is expounded with attention to the convergence of the process and the estimation of error. Rather more advanced theory begins in the fourth section, which studies variational methods: the Rayleigh-Ritz method, first fully elucidated by N. M. Krylov, and the related but somewhat simpler and more general method of Galerkin, are fully explained and exemplified. The fifth and sixth sections form a compact treatise of 250 pages on the theory and applications of conformal mapping; the reader is supposed to know the elementary ideas as far as Riemann's theorem on the existence of a conformal mapping between two simply connected domains. The boundary-value problems of Dirichlet and Neumann, and for the biharmonic function, receive thorough treatment. There are numerous examples, though, for the biharmonic problem, the reader is naturally referred to the many and varied applications of the method made by Muskhelishvili in his excellent book on elasticity. It may be noted that Muskhelishvili refers to Kantorovich and Krylov as a classic work on the application of complex variable methods, and the two books resemble one another closely in spirit and in technique. The final section gives Schwarz's method of solving Dirichlet's problem for a complicated domain by combining solutions for simpler domains: the method is illustrated by the complete solution for an L-shaped domain.

As a compendium of methods available in 1940, and as an instance of what can be done by skilfully combining general theory with numerical analysis, this is a noteworthy volume. It should be interesting to see how future revisions are modified by the increasing dominance of the automatic computer. The translation, by C. R. Benster, is fluent: the bibliography unfortunately makes no serious attempt to include non-Russian material. T. A. A. BROADBENT

THE THEORY OF PRACTICE

Planning of Experiments

By Dr. D. R. Cox. (Wiley Publication in Applied Statistics.) Pp. vii+308. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd., 1958.) 60*s*. net.

DR. D. R. COX succeeds well in his aim of writing an introduction to modern thought on the design of experiments free from the statistical and mathematical technicalities that often discourage the experimental scientist from study of a subject so inportant to his own work. He says much about the nature of computations required in the analysis of experimental results without presenting one analysis of variance table. He displays a wide range of standard experimental designs, and discusses their uses, while saying little about how to construct them or about mathematical theorems relating to their existence.

Although an increasing number of scientists has sufficient knowledge of statistical practice to learn about experimental design more intensively than this approach permits, undoubtedly many others will profit from it. The book could be an admirable introduction to statistical ideas for a biological or industrial scientist; from it he would learn little about the standard procedures of statistical analysis, such as are to be found in most elementary text-books, but he would acquire something of greater practical value, an appreciation of the manner in which the design of an experiment affects the precision of the results and the efficiency with which the experimenter's time and resources are used.

Dr. Cox's book is far more than an introductory text. With the exception of Davies, probably no writer on design has given comparable attention to questions of general planning, such as the choice of treatments and levels for testing, of experimental units, and of measurements. Anyone concerned with experimental statistics can benefit from studying, for instance, the sections on types of factors and interactions and the choice of factors for inclusion in an experiment. An excellent and varied collection of examples will make the book also of value to the teacher.

The only serious blemish is the conversion of 6.25 dollars into a British price of 60 shillings.

D. J. FINNEY

Bertil Hanström

Zoological Papers in honour of his sixty-fifth Birthday, November 20th, 1956. Edited by Karl Georg Wingstrand. Pp. 312. (Lund: Zoological Institute, 1956.) 50 Sw. Kr.

SCRUTINY of these papers soon reveals that they mark more than a formal occasion. In offering them to Prof. Bertil Hanström, the contributors have taken obvious pleasure in expressing their gratitude to him " . . . as a teacher and leader of the Zoological Institute in Lund".

Prof. Hanström's first paper was published in 1915, and it dealt with the birds of the island of Öland. While his subsequent work has been mainly concerned with nervous systems, particularly with neurosecretion, Hanström still finds time for field studies. It is thus not surprising that Lund is now an important centre for systematic, zoogeographical and ecological work.

Hanström's interests are clearly reflected in this series of papers. As might be expected, there are several papers on neural and neurosecretory systems (concerning insects, chilopods, crustaceans, cephalopods and the toad, *Bufo bufo*). Others deal with the systematics and relationships of crustaceans, ecology and cytology. The range of these papers shows clearly that zöology is in a flourishing state at Lund.

The contributions are nicely produced and bound, the design for the cover being particularly appropriate.

N. B. Marshall

Diagnostic Performance Tests

A Manual for Use with Adults. By Boris Semeonoff and Eric Trist. Pp. xv+176+4 plates. (London: Tavistock Publications, 1958.) 32*s*. net.

AS is well known, intelligence tests were evolved in order to detect and assess educationally subnormal schoolchildren. Their intention was to sample mental growth in its various aspects and to provide reliable standards of performance in relation to age. By and large they succeeded admirably. In the case of adults, on the other hand, mental testing has proved altogether less satisfactory. Although a wide variety of tests purporting to measure adult intelligence exists, it is seldom clear precisely what is being measured or how much confidence can be placed in the results. In consequence, the use of intelligence tests with adults has been viewed—in Britain at least—with understandable reserve.

The methods of testing intelligence described in this book have an unusual history. In 1940, Mr. Trist was concerned to develop some tests of intellectual deterioration due to injury or disease of the brain. In the light of the work of Goldstein and others, it had become plain that such deterioration is particularly liable to show itself in performances involving abstraction, spatial analysis and sequential learning. Mr. Trist was therefore led to devise a small battery of tests well adapted to reveal defects in these fields. But it soon became clear not only that extensive control data were necessary but that the techniques might have important application to the assessment of healthy individuals. At this point Dr. Semeonoff entered the picture and was able to carry the work very much further. Indeed, the present book is very largely the outcome of his prolonged and patient endeavour.

The performance tests reported here have the advantage first, that they make little demand upon linguistic sophistication; and secondly, that they permit some evaluation of important aspects of personality. Indeed, the emphasis throughout is upon assessment of the individual as a whole rather than upon some arbitrary dimension of intellect or temperament. In consequence, these tests may be expected to find application not only in clinical psychology but in any field of personnel selection in which considerations of temperament are relevant.

This battery of tests is perhaps the first to be evolved in part at least on a neurological basis. If it be conceded that the brain has at any rate something to do with intelligence, this would seem a notable—if belated—achievement.

O. L. Zangwill

A Study of Blackbirds

By Dr. D. W. Snow. Pp. 192. (London: George Allen and Unwin, Ltd., 1958.) 21*s*. net.

BEFORE the natural history of a wild species can be understood it must be studied from more than one point of view—only when behaviour, ecology, systematic position and other aspects of its biology are inter-related can a full picture be obtained. This book describes a study in which much progress has been made in this direction. Based on four years work in the neighbourhood of the Botanic Garden, Oxford, it presents intimate details of the history of a small community of blackbirds, many of which were colour-ringed. Although written in non-technical language (much of the material has also been published in scientific journals), the author places his observations against a wide background of biological principles, and thus provides material both for the general ornithologist and for professional biologists.

As well as descriptions of the life-history, displays and vocalizations of the blackbird, many interesting facts which could have come only from a close study of colour-ringed birds are presented—for example, the pairs which are sometimes formed in winter are only temporary affairs; and male and female feed different individual young after the brood has left the nest.

Perhaps the most interesting chapters are those which deal with population problems. In particular, a contrast is drawn between garden and woodland populations. The former are dense, with a high breeding success, and produce an excess of young birds which do not disperse before settling. Under these conditions, territorial behaviour limits breeding density. Woodland, on the other hand, is sparsely populated, and breeding success is low; population density is probably controlled largely by survival in the preceding winter.

R. A. Hinde

Proceedings of a Symposium on Insect and Food-plant

Wageningen, May 27–29, 1957, under the auspices of the Comité Européen de Zoologie Agricole (C.E.Z.A.) and the Agricultural University, Wageningen. Pp. 118. (Wageningen: Landbouwhoogeschool Laboratorium voor Entomologie, Berg 37, 1958.) 5 florins.

SYMPOSIA are becoming increasingly used as a means of communication between scientists; subsequent publication of the reviews and discussions often go far to help the research worker to keep abreast of the latest ideas and results of others. According to the preface of the proceedings of this symposium, the organizers had hoped to obtain during the discussions "a synthetic view of the whole complex of insect – host-plant interactions". Although this aim was, unfortunately, not achieved, the articles are a useful survey of recent work which every agricultural entomologist will want to have by him.

The symposium was held under the auspices of the Comité Européen de Zoologie Agricole and the Agricultural University, Wageningen, under the presidency of Prof. B. Trouvelot. The contributors came from six different European countries and one came from Canada; their articles are in English, French and German, most of which have a summary in one of these languages. Ten of the fourteen articles have already appeared in Vol. 1 of the new journal, *Entomologia experimentalis et applicata* (*Nature*, 181, 1040; 1958).

The emphasis of the symposium was on food-plant selection and the resistance of host-plants to phytophagous insects. Six articles deal particularly with the Colorado potato beetle which has received much attention from European workers in whose countries it is a serious pest; work on host-plant resistance to the beetle among the Solanaceae and on the behaviour of the larva is reviewed. Two papers are concerned with aphids, and one, by a botanist, reviews the related subject of phloem sieve tube sap. One contributor discusses the significance of the salivary secretions of 'plant-sucking' Hemiptera, and another, in a brief summary (in German), deals with his work on the choice of food by certain lepidopterous pests. Two articles on the potato-root eel-worm are included on the grounds that the problems of the nematologist are similar to those of the agricultural entomologist, but an article on the dietetics of a blowfly appears to be somewhat out of place. C. J. BANKS

Instrument Encyclopedia

Compiled by Edward W. Battey. Pp. xix+292. (London: The Herbert Publishing Co., Ltd.) 63*s*. net.

THE purpose of this book is defined in the preface as follows: " . . . to provide a concise reference to the materials and equipment used and produced in the Instrument Industry . . . and to define the terms employed and required by instrument users in every industry. The Encyclopedia is not in any sense intended as a text-book. . . ." The compiler has realized these aims remarkably well.

The book starts with a detailed index and a short but well-planned encyclopædic section explaining meanings of technical terms. It includes some of the near slang expressions which have found general use, and references are given, where appropriate, to British Standards specifications. The remainder of the book consists of alphabetical lists of manufacturers, complete with their addresses and telephone numbers, a list of overseas agents, a catalogue of trade names and an extremely full buyers' guide. This last section is the largest and perhaps the most useful. It permits one to discover the manufacturers of any specific instrument or component, and is divided into eight sections (Laboratory, Medical and Research; Optical and Ophthalmic; Electronic and Nucleonic; Electrical; Engineering; Automation and Process Control; Accessories and Components; Nautical, Aeronautical and Surveying.)

In order to make some kind of assessment of the completeness of the information a number of 'spot tests' have been applied, and the "Encyclopedia" survived most of them with flying colours. It defeated many attempts to think of lesser known firms or instruments which, though not included, should legitimately come within its scope.

The only real criticism to be made is of the title. One usually thinks of an encyclopædia as a collection of explanatory information: the actual encyclopædic section of this book is only 28 pages long and perhaps it would have been wiser to choose a title more in keeping with the remaining 264 pages. However, it will undoubtedly prove a most valuable work of reference, particularly for those needing to use apparatus and instruments not closely allied to their own field of work. C. A. TAYLOR

Dictionary of Physics

Compiled and Edited by H. J. Gray. Pp. x+544. (London and New York: Longmans, Green and Co., Ltd., 1958.) 84*s*. net.

THERE are obvious difficulties in reviewing a dictionary since the reviewer can scarcely be expected to read it from cover to cover. But 'spot' checks in several different branches of physics showed very few weaknesses; only a few items sought (synchrocyclotron, photo multiplier, Fermi surface) were not found. In general, the definitions are clear and concise, and references are given for follow-up reading. Perhaps the policy of giving only the earliest references is unwise, even if historically they are the most important.

A few mistakes were found: the diagram of the spherometer is described as that of the planimeter; the last sentence of the entry for Laue is wrong; a sign convention in optics is called the 'real position' convention. But on the whole the number of such mistakes appears to be small. The reviewer is glad to note that the dictionary insists on the correct spelling for Abbe (not Abbé) and is not caught out by Kirchhoff; it also ascribes Bragg's law to the correct Bragg.

The dictionary may thus be described as an extremely useful work. It is obviously not perfect; but it will form a handy work of reference for any physicist. H. LIPSON

Zirconium

By Dr. G. L. Miller. Second edition. (Metallurgy of the Rarer Metals, No. 2.) Pp. xxi + 548. (London: Butterworths Scientific Publications; New York: Academic Press, Inc., 1957.) 70*s*.

FIRST published in 1954, this important work of reference on the manufacture and properties of zirconium has been considerably re-written and enlarged with an increase in the number of pages from 374 to 535. The price of the book has also increased from 45*s*. to 70*s*.

Dr. Miller has made some reconstruction to the text and the arrangement of the matter and has taken advantage of relaxation of classified information in various directions, and added a considerable amount of new data.

The principal additions are in the description of the Kroll process, in the description of the thermal properties and the tensile properties of zirconium, and in the description of the mechanical properties of certain zirconium alloys. The section on corrosion of zirconium by liquid metals has been expanded substantially and the number of pages devoted to melting practices has been doubled. There have also been additions in connexion with the fabrication processes for zirconium and in the description of the nitrides, carbides, borides and silicides.

This book represents the best compilation of information on this subject at the present time. W. D. JONES

THE AMERICAN COLLEGE AND THE EDUCATED LIFE*

By Dr. DOUGLAS M. KNIGHT
President of Lawrence College, Appleton, Wisconsin

THE Rockefeller Institute lends and can lend unique distinction to our image of the educated man; but that image could not properly exist without a widespread and deeply rooted sense of what goes into his creation, encouragement, and nurture. The community of graduate scholars at its finest is not possible unless there stands prior to it the community of those who may some day be scholars.

The mandate to create a climate for liberal learning has been alive in most undergraduate colleges since their beginning. Their frontier setting, their financial struggles, at times their narrow sectarianism—none of these things should blind us to the fact that their very foundation in the midst of so much uncertainty was a major act of faith, and faith in the same qualities of inquiry, judgment, commitment which two hundred years earlier had led to the founding of the country's oldest college. Fortunately for American intellectual development as a nation, many of the nineteenth-century undergraduate colleges have remained true to a version, at least, of their original duty. To say so implies no criticism of those which have become world universities during the last century, but a Harvard, a Yale (or a Rockefeller Institute, for that matter) owes much of its opportunity for great achievement to a group of small, less privileged institutions which in the last hundred years have developed the art, the science, and the community of distinguished undergraduate education. The context of the houses at Harvard and the residential colleges at Yale is not merely the tradition of Oxford and Cambridge; it is equally the tradition of the American college.

I sometimes hear it said that in the harassed world of to-day and to-morrow the undergraduate college will have a precarious and uncertain time; those who make the remark do not know the history of these colleges, which in a sense has always been precarious; nor do they remember that any great cause must have elements of the precarious and uncertain about it. The history of the American college at its best is a history of steadily increasing strength, of increase in intellectual range and sophistication without the sacrifice of coherence, of increase in duty to the country without the sacrifice of local obligation.

The gravest danger in the years ahead (and if it is a danger to the colleges it will be an equal menace to the great communities of graduate study) is not the danger of financial bankruptcy or depleted faculty. The greatest danger will come from the more subtle and more pervasive issues which involve our whole society—the steady shift towards a national uniformity in culture, the equally steady diffusion of residential communities, the explosive developments of knowledge which often outdate our perception before we have time to master it. These shifts will stand behind the real crises of undergraduate education in the years just ahead of us. These are more critical issues for the college than for the university, simply because the college depends for its life on the real and daily community of those who learn, and equally on the orderly assimilation of the major disciplines and the major modes of understanding. A great university to-day often assumes (for better or worse) that it is not one community but many; it assumes equally that it has a primary obligation to the growing edge of knowledge in a hundred fields, rather than to the full assimilation of knowledge either within these fields or between them. Such assumptions would be fatal for a college; it must face instead a question in some ways more complex than the university question. It must maintain the community of learning both in idea and in fact; it must affirm and sustain the steady growth of knowledge, while equally it must maintain the coherence of knowledge. Both in its sense of community and its approach to learning, it must avoid the cold death of being academically outdated on one hand, or the fiery end of being intellectually fragmented and shattered on the other. Unless this balance of forces can be sustained, the distinguished liberal colleges will obviously suffer in the next twenty-five years; and if they do fail in their attempt at coherence, the damage to the university and the graduate research centre will be greater than most of us realize.

The hope and destiny of the learned life cannot be confined to one type of institution, or one advanced level of performance, no matter how superb. The scholar who cannot depend upon a climate of respect in his society will not long be able to guarantee his scholarship: and since the live interchange between the scholarly life and the whole life of society occurs nowhere else so effectively as in the undergraduate years, it may not be totally arrogant to say that the future of the Rockefeller Institute rests partially in the power of a hundred liberal colleges not only to provide graduate fellows but also to maintain the climate of learning in the United States—even for and in those who themselves will never be learned men or women.

If this is so, however, then any college of stature is faced with a triple responsibility: first, for the education of those who are destined to be scholars; secondly, to the sense of coherence in knowledge without which true learning soon becomes impossible; and thirdly, to the national climate of respect for learning which must constantly increase if the learned life is to keep pace with the terrifying growth of American society. How are these things being done, and how are they to be done in the years ahead?

Two chief means are available to the college: the first grows from a formal pattern of study, the second from the living fact of an academic community. I assume that there is no uniquely effective curriculum, and no perfect community. If we look at the ends of formal education rather than its means, however, we do find a certain uniqueness of purpose in the liberal college. It assumes above all that the great traditions of knowledge and its emergent patterns have much to do with one another; that the study of Plato, for example, and mathematical theory of government, and contemporary nationalism in India may have something crucial in common. If it is to be worth anything, this sense of continuity must look with an equal eye on the genuinely new and the permanently valid; it must represent the true and persistent relationship of many minds at many times, while it maintains its final allegiance and its deepest reverence for the timeless moment of discovery which flames only in the individual mind.

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* Substance of an address delivered on May 21 at the Rockefeller Institute Convocation for Conferring of Degrees and Dedication of New Buildings (see also *Nature*, 183, 1629; 1959).

To say this is, of course, to imply that the curriculum of the liberal college cannot be regarded as an end in itself; whatever its formal content, whatever the means it uses to guarantee the continuum of knowledge, a course of study has its meaning only if it assumes life in the individual; it is the single person who is the true unit of education—not always a person alone, but still an individual, no matter how many times he is multiplied in his community. The great curse of size and mass in education is that they blind us to the end, and lead us instead to talk endlessly about the process. The process of education is no substitute for the educated man; in a sense the greatest responsibility of liberal education is to keep its process simple enough so that the event of true education can still occur.

If this event of education involves the individual, it also involves something very special about the individual, that is, his power to create. It is a great pity that the nineteenth-century encouraged its artists to pre-empt the language and idea of creativity; for there is no difference except one of mode between true insight about the order of protein molecules and that true insight of the poet which James Joyce describes as "his own rare thoughts, a chemistry of stars". There is no difference, except one of degree, between the subtle and distinguished perception which adult intellectuals are capable of and the first fumbling recognition by a child that the black lines on a page somehow represent reality.

In all these cases the creative mind is proving itself, alive in the individual and working with the continuum of knowledge, and it is actually this living triad of individual, creative insight and tradition of knowledge that makes the liberal college a major force in the intellectual life of our time. Any one of the three, or any two, would fail to provide that explosive encounter with the intellectual life which is the hallmark of true education as opposed to dead learning or technical discipline.

This encounter in turn both creates and is created by a particular kind of community. Historically, of course, the undergraduate college had about it the inevitable and simple order of Plato's academy (often, alas, without Plato); but the thrust of our society has put upon it a duty not imagined a century ago. As the great cities have sucked in millions of people, and then flung them out again to spawn in suburbia; as transportation has made the means of movement easy and the ends more and more obscure; as migration has become the norm of social life and not just a function of the frontier—as all these things have taken place, we have found ourselves confronting, not the regional social order that sustained us a century ago, but a national and indeed supra-national order within which we must somehow find a path. Regional order gave firm, even if narrow, support to the individual; but our struggling world order is a threat instead. It forces upon each of us the necessity to define ourselves, to establish our powers and our commitments, and then to use our talents in the service of a society that does not yet exist. We must realize that to-day we shall not find encouragement toward intellectual excellence anywhere unless we find it in academic community. Where once we could share the responsibility with many other aspects of society now we must carry it ourselves in the undergraduate colleges and the great graduate centres of learning.

As a result we have substituted in education a new frontier for the old, a frontier of the mind to replace our old frontier of physical expansion. To put the matter another way, where colleges and universities once reflected their culture, they must now create, establish and confirm it. As our society has cast off all sense of its own coherence, we have assumed the burden of creating coherence again, and often in the face of scorn or even angry opposition. The intellectual obligation of the college is equally in our future a moral and social obligation.

This obligation will be met in many ways, of course, but above all through the unique power of the undergraduate college to bring together qualities of mind and person which are often kept apart by the rest of our society. I shall mention only three of these complex qualities, and I shall represent them by a pair of what I might call 'related opposites': first, knowledge and immediate experience; secondly, tolerance and commitment; thirdly, individuality and community. In each case one half of the equation—knowledge, or tolerance, or individuality—is commonly regarded by our society as somehow less significant than the other half—immediate experience, or commitment, or communal life. It is the insistent claim of the best education, however, that we cannot participate in the immediacies, the commitments, the communities of our world until we understand them; but it is our equal claim, of course, that we fail just as badly if we give our allegiance only to a passion for abstract knowledge, only to a tolerant but therefore detached appraisal of human convictions, only to the existence of the individual and not to his relationships. The educated life expresses itself above all in a victory over these polar attitudes; it sees that wisdom can come only from the fusion (not just the co-existence) of learning and experience; it sees that responsible society can only be based on the interaction of single life and common purpose; it sees that neither wisdom nor society can long survive unless we give our equal allegiance to our own final convictions and to our respect for the convictions of others. It is the power and the duty of the best education to show that these 'related opposites' are essential to one another if the life of the mind is to flourish, and equally if the life of the community is to be possible.

I can put our responsibility best, perhaps, by saying that though these disparate human qualities need to be brought to a common life in every aspect of our society, it is only the undergraduate college, with all its pedantries and all its social follies, that can take full advantage for this purpose of a discipline of study, an intimate community, and a uniquely formative period in life. Our most singular institutions and traditions—our faculty determination to give all the wrong issues the most heated discussion, our student obsession with freedom and fumbling at responsibility, our trustee rule which combines amateurism so curiously with final control—all these things which are the material of vitriolic novels are really not the base for satire at all, but the base instead of a way of life and a definition of the mind. Without faculty independence, student freedom, or trustee non-professionalism the need to reconcile opposing attitudes and judgments would never arise, and the real nature of a democratic society would never become integral to the college. We would then be machines devoted to instruction ; instead it is our pride that we are living institutions devoted to education.

From the struggle, the diversity of judgment which are the heart of the liberal college we derive, not only the organic nature of the place but also its power to foster creative life and a sense of community. Neither of these central human concerns can exist except in a setting of freedom on one hand, and the desire to make order out of freedom on the other. Mere freedom leads us to chaos ; mere order leads us to decay. The life of the mind, and the life of true community move constantly between the two extremes, creating an order, throwing it away in the profound conviction that a better order can be found, recognizing that neither freedom nor order can be allowed to exist without the other. The philosophical and indeed theological base of all valid education consists in this perhaps ; a firm enough faith in the final values so that we can endure all kinds of darkness along the way, but a recognition that without the darkness we shall never grow in wisdom or community at all.

One of the most tragic aspects of our 'public culture' at the moment is precisely its fear of this creative darkness. We are conscious enough of the other kinds of darkness, those that lurk always at the edge of foreign policy, stare out of a mental hospital or up from the sidewalks of a slum. The darkness of unknowing, however, makes inner demands on us which we prefer to ignore or to escape ; our pride will not accept the dark humility of ignorance, and we forget that it is the only prelude to knowledge. We are willing as a society to repeat the most trivial newsprint version of reality rather than puncture with a question our own pretences at understanding.

In the face of so much bogus knowledge and so little real wisdom it is our place in the liberal colleges to maintain above all that the educated man is the man who will move ahead of his learning, not the man who hides behind it. This man, whom, we hope, we have some share in creating, lives out again and again the central paradox of the Hebrew-Christian tradition. He saves his life by losing it ; he risks his security by giving himself to a new idea, an untested theorem, a change of heart. He takes the chance of being wrong, in the faith that the only unforgiven sin is the lack of enough courage to take that chance. Every true community, and every living idea, are the results of just such courage ; and it is the central task of the liberal college to foster it, develop it, and make certain that it thrives in our society.

If I am at all accurate in this estimate of the best undergraduate education furthermore, I have also been describing the major responsibility of the Rockefeller Institute. The setting is different, the measurable task is more complex in certain ways ; but its twin bases are the creative intellect and the living community. More is expected than the advancement of knowledge, more than the interaction of the great scientific disciplines. When the first graduate Fellow was added to the community of scholars at the Institute, two new responsibilities were assumed : first, for the continuing life of the mind as something shared equally by scholar and pupil ; and secondly, for a public image of academic achievement as inseparable from the worthy ends of society at large. The Institute is an instrument of public policy as well as private research ; it embodies a way of living as well as a way of knowing.

There have been times in Western society when this way of living (the way of the best undergraduate colleges, and the strongest graduate centres) was not as important as it is to-day, and as it will be in the next half-century. It is a commonplace, but a crucial one, to point out that we are in the midst of a world revolution. Not quite so taken for granted, however, is the fact that this revolution involves every aspect of our internal as well as our external life ; and recognized scarcely at all is the fact that only the awareness and conscience of educated men can give us any hope of turning this revolution to creative ends rather than destructive ones.

The truth of the matter, however, confronts us wherever we turn. The tragic recent tangles over national security, for example, almost succeeded in destroying the tradition of responsible dissent. For a year or two many of us were faced with the specious choice between dictated conformity and scorned or discredited independence. We forgot that our political tradition demanded of us loyalty *and* freedom, not loyalty *or* freedom ; and in forgetting this we ignored the first mandate of the educated life, that we learn to live with the painful complexity of the truth: and we have made the same error in our social order, of course ; we tend to assume far too easily that our social hope and purpose are tied to our progress from group to group ; the conflicts which we allow are the thoughtless conflicts of one conformity with another, rather than the thoughtful and productive conflict between individuals and their social order.

Those of us in the academic life are no more exempt from these conformities than our neighbours in industry or government. We have our own clichés, of course, but too commonly we are their victims rather than their masters : and this is true not only if we scrutinize our participation in the social structures of our time but also if we look honestly at our own professional commitments. We assume far too easily that the truth has a departmental structure to it, and as a result we run the constant risk of scattering and dispersing the creative centre of knowledge, which lies primarily not in learned information but in learned interpretation, not in the fragmenting of reality but in its understanding. Here again, learned insight means little until it becomes educated insight, until its real purpose is the mastery of what Yeats described as "the bitter fury of complexity".

The most obvious and insistent demand on educated insight to-day comes, as all of us know, from our emerging international relationships. Here we face in its clearest public form the question which privately animates every true scholar, student, citizen ; how I am to keep my identity, my own sense of significance, while I do proper justice to the identity of others ? It is this failure as a nation quite to believe in the identity of others that has caused some of our major difficulties in the last fifteen years ; and we shall solve them only if we bring to the task of creating foreign policy the most aware and charitable insights of our best-educated minds.

All these areas in which policy and performance must grow creatively are aspects of that central revolution of our time which is a revolution in value. The struggles of a hundred societies to-day are dedicated, not to the simple overthrow of everything that has been believed in the great cultural traditions, but to the radical reassessment of every basic conviction about the nature, purpose, and proper conduct of human life. If we try to pretend that anything less than this is demanded of us by our time, then we have not even begun to act like educated people. We must affirm in the boldest way that the demands of the future are demands above all upon the mind and spirit, and that they can be met only by the deepest efforts of which the educated mind and the learned heart are capable.

THE ROLE OF THE SCHOLAR IN SOCIETY

A SYMPOSIUM under this title was held in Tunis during April 13–18. There were twenty-five invited participants, drawn from fourteen different countries; the study group meeting was organized by the Committee on Science and Freedom, of which the chairman is Prof. Michael Polanyi. The meeting was one of a series of international seminars under the general title "Tradition and Change—Problems of Progress," financed by a special grant from the Ford Foundation to the Congress for Cultural Freedom. This is an international cultural organization with headquarters in Paris, which finances the activities of the Committee on Science and Freedom.

The meeting in Tunis was concerned with the special problems of new (or newly expanded) university institutions in the rapidly developing regions of Africa and Asia, including the Arab countries of the Middle East, and in particular, with the proper relationship between these universities and the society which they serve. Tunisia is a rapidly developing African country which is planning to establish a new university, and a gratifying feature was the interest shown by the Tunisian Government, coupled with the active participation of the Tunisian members of the study group, notably Prof. Ahmed El Fani, of the Free University of Tunis, Mr. Lamine Chabbi, a former Minister of Education, and Mr. Mahjoub Ben Milad, head of the teachers' training college. The chairman of the study group was Dr. J. W. Cook, vice-chancellor of the University of Exeter, and much of the discussion centred on papers which had been prepared in advance by some of the participants.

The Tunisian Minister of Education, Mr. Mahmoud Messadi, presided at the public inaugural session, and in a stimulating and scholarly address referred to Tunisia's cultural background, and outlined the rapid educational progress which has been made since independence, and the plans for future development. Already about a fifth of the national income is being spent on education; nearly half the children now receive primary education, which is expected to become universal within the next ten years. There are several institutions of higher education, including a training college for secondary school teachers, a traditional Muslim university, and the Institut des Hautes Études, affiliated to the University of Paris. Some of these will constitute the nucleus of the new university. In a subsequent session, Mr. Chabbi gave a more detailed and penetrating analysis of the prospective functions and scope of the new university, closely in line with the traditional concepts of a university of Western Europe. He emphasized the need for autonomy, and stressed the importance of vocational guidance with a view to a satisfactory distribution of students among subjects at a time when, for example, the demand for engineers and technicians could absorb the entire output of the secondary schools. He envisaged the university as a lively institution orientated to the service of the community, its research activities being planned in co-operation with consultative bodies representing government and industry.

Prof. B. A. Fletcher, vice-principal of the University College of Rhodesia and Nyasaland, went even further in his concept of the social functions of a new university in a new country, and indicated how the institute of education under his direction provided an advisory service for the government and for industry. This view was challenged by Prof. Polanyi who, while accepting the principle that individual members of a university might be available for consultation, insisted that the university as a body should not attempt to offer authoritative opinions. He remarked that the Royal Society had long since found it expedient to refrain from giving a collective opinion on scientific matters on account of its earlier unfortunate experiences. Prof. Polanyi also disagreed with the suggestion of Prof. Fletcher that the great discoveries of modern physics have been the result of team work. According to Prof. Polanyi, all the great scientific discoveries are individualistic. He was sceptical about the feasibility of control and co-ordination of research, and claimed that research in the natural sciences is self-co-ordinating. Scientific discovery depends on the reliability, the systematic character and the intrinsic interest of the work. He defined the fields of enquiry for which the university is the only place, and those, stimulated perhaps by the possibility of practical application, which may also properly be carried out in the university. Unsystematic technology and invention, he thought, should have no place in the university.

Prof. E. G. Malherbe, vice-chancellor of the University of Natal, referred to the industrial research institutes established in association with his university, the head of the institute being given professorial rank. This helped to interest students in careers in industrial research, and the institutes often encountered long-term theoretical problems suitable for academic study in the appropriate university departments.

There was much discussion about the claims of society on the university in a new country, and how they could be met in ways consistent with academic freedom and university autonomy. Much was said about the pressures liable to be exerted for control by government of the output of teachers, engineers and other professional personnel; of the pressure to increase numbers and to reduce the length of courses in the interests of more rapid output. It was agreed that such pressures should be resisted. But although there seemed such general agreement about these principles in the abstract, one had the impression that different members of the study group interpreted them variously, in the light of the circumstances of their own countries. It is not surprising that the attitude of the community to the university in a poor and rapidly developing country is inclined to be more utilitarian than in a country where both the community and the university form part of an old established order. However, in the last analysis, as Dr. Salwa Nassar, of the American University of Beirut, so aptly remarked, the role of the scholar in society is to be a scholar.

Prof. Ehsan Naraghi, of the University of Tehran, wondered if pure research was too much of a luxury in an under-developed country. This brought a spirited rejoinder from Prof. Edward Shils of Chicago, who insisted on the need to have in the university the stimulus of taking part in extending the frontiers of knowledge. There was, perhaps, insufficient attention given at the meeting to the criteria for establishing and maintaining academic standards.

In such a gathering at such a place, constantly recurring themes were, not surprisingly, the influence of religion and the problem of language. Dr. Romila Thapar thought that authoritarian religious traditions in India had promoted an attitude in the student of unquestioning acceptance. Mr. M. Bashir was even more gloomy about the stultifying influence in Pakistan of this authoritarian concept of education. As this was linked with the Islamic religion, his views were hotly contested in a meeting where the Arab countries were strongly represented. An interesting point which some had not appreciated was that the problem of the language to be used as the medium of instruction was not the same problem in the Arab countries, as it is in India, for example. In the latter case the choice is between English and a synthetic national language, Hindi, bearing little resemblance to the host of different languages in use in different parts of the country.

In the Arab countries, there is a single national language and the choice is between English or French, and Arabic. In Tunisia the matter had been virtually decided by the decision of the Government to adopt bilingualism (Arabic and French). Mr. Cecil Hourani, adviser to President Bourguiba, made a strong plea for the simplification and clarification of the Arabic language. Attempts to give a complete education in the Arabic language, as is attempted at Damascus, cannot be successful, he thought. Re-fertilization of the Arab mind can take place only by contact with non-Arab sources. This view did not pass unchallenged, and the Arabic language was defended by the Lebanese Ambassador to Morocco, H. E. Selim Haidar, who claimed that Arabic is by its nature a scientific language ; he thought that an Arab student would gain just as much from instruction in modern science in Arabic as in a Western language. Interesting views were expressed by Mr. Cecil Hourani, and by his brother, Mr. Albert Hourani of Oxford, about the present and future roles of the three types of university which are found in some countries of the Middle East ; namely, the traditional Islamic institutions, the 'foreign' universities, such as the American University at Beirut ; and the modern State universities. Only the latter were thought likely to survive as significant influences in the national life.

The idea of a 'foreign' university out of touch with indigenous culture, nationalist sentiment and tribal loyalties was evidently in the minds of the two Nigerian contributors from Ibadan—Dr. E. Njoku, who sent a paper, and Dr. H. A. Oluwasanmi, who attended the meeting. Nigeria demanded a university as good as those in other countries. If academic freedom is a necessary element, then it must exist in Nigeria. But the principle of academic freedom is too shallowly rooted to withstand the over-riding claims of the tribe. Cultural activities, being largely European, make the university seem more exotic than it is, and this causes resentment.

The Turkish participant, Mr. Osman Okyar, suggested that the wave of nationalism which accompanies independence may be a passing phase, and he instanced the support now being given by his Government to university institutions of foreign origin.

The Tunis seminar provided a forum for a useful exchange of views on problems which were approached from several different points of view, and the full publication of its proceedings, which is expected later, will be of interest to all who are concerned with higher education in the emergent countries of Africa and Asia.

J. W. Cook

RADIOACTIVE FALL-OUT

THERE have been four important and authoritative statements on hazards from man-made radiation : a report by the Medical Research Council in Britain, published in 1956[1]; a report by the U.S. Academy of Sciences, also published in 1956[2]; a report by the United Nations Scientific Committee on the effects of atomic radiation, published in August 1958[3]; and a statement on this last report by the Medical Research Council, which appeared simultaneously with it[4]. In a statement which the Prime Minister circulated in the Official Report of the House of Commons (*Hansard*, April 28) he refers to the United Nations report ; but his own statements, and in particular those publicized by the Press, are mainly based on the first of these publications, which in some respects has become obsolete.

This is particularly true of the ratio 100 : 22 : 1 (or somewhat more than 1), which plays such a prominent role in the Prime Minister's replies. It is said to be the ratio between the amounts of radiation received (*a*) from natural sources (background radiation), (*b*) from medical and industrial uses, and (*c*) from fall-out due to nuclear bomb-tests. For several reasons this ratio is no longer valid. First, the Medical Research Council has meanwhile revised its estimate of the dose of radiation which the average individual receives through X-radiation. In concordance with the estimate made in 1956 by the U.S. Academy of Sciences, the Medical Research Council in its 1958 statement admits that in countries with highly developed medical services the amount of radiation from diagnostic X-rays may well be as high as the background radiation. In other words, the ratio between the first two items may be 100 : 100 instead of 100 : 22.

For the discussion of radiation hazards from bomb tests this is relevant, because certain radiation effects are cumulative, and even if X-rays should be used more sparingly in the future, a high amount of X-radiation will have to be reckoned with as an unavoidable ingredient of civilization. It should also be pointed out that, contrary to the Prime Minister's statement, these figures (22 per cent in the older report, 100 per cent in the newer) refer only to diagnostic X-rays, and include neither therapeutic nor industrial radiations.

Secondly, when the Prime Minister states that radiation from nuclear bomb tests amounts to 1–2 per cent of the background radiation, it is not clear to what he refers. At the present time, there is a constant increase in the amount of fall-out, and figures which are valid in one year will be too low already in the next. The Medical Research Council report of 1956 estimated that, if bomb tests were to continue indefinitely at the then existing rate, an equilibrium between formation and decay of radioactive matter would be established in about a hundred years and that in this equilibrium state radiation from fall-out would be approximately 1 per cent of that produced by natural sources. However, a warning was given that this might represent an under-estimate if "present rates of firing were increased and particularly if a greater number of thermonuclear weapons were tested". From the fact that strontium fall-out during the past year has increased far beyond expectation, we may suspect that this warning is applicable, and that the 1956 estimate of fall-out rate at equilibrium was an under-estimate.

Cæsium-137, Carbon-14 and Strontium-90

There is a further reason why the Prime Minister's estimate of man-made radiation is too low. This is the discovery of two more radioactive elements in fall-out, namely, cæsium-137 and carbon-14. The former had just been discovered when the 1956 report of the Medical Research Council came out. It is briefly mentioned in this report, but its effects are not included in the estimate of fall-out. In the United Nations Report this omission has been amended, and the final figure for fall-out radiation, if tests should continue at the present rate, is several times as high as that quoted in 1956 by the Medical Research Council, which accepted this higher figure in its 1958 statement. This means that the amounts of radiation received at equilibrium from natural sources, from diagnostic X-rays (*not* including radiotherapy and the use of radiation in industry and research) and from fall-out are estimated to occur in the proportion of 100 : 100 : between 2 and 4. However, even this is still an under-estimate of the amount received from fall-out; for quite recently—too recently to be mentioned in the United Nations Report—carbon-14 has been found to be present in fall-out from nuclear explosions. According to Prof. L. Pauling, carbon-14 is by far the most dangerous component of fall-out, because it is produced in large amounts at nuclear explosions and takes thousands of years to lose its radioactivity.

It should be stressed that strontium-90 is peculiar in its effects in that it is taken up selectively into the bones, especially those of growing children. The amount so taken up is evidently related to the amount coming down in rainfall, but the relationship is far from straightforward. It depends on the type of soil and vegetation in the fall-out area and on the kind of food by which it is introduced into the human body. The United Nations Committee estimated that for the same amount of fall-out the average concentration of strontium-90 will be five to six times as high in the bones of peoples living mainly on a plant diet than in those of peoples with a milk-type diet. The Medical Research Council accepted this estimate in its statement.

Biological Hazards of Radiation

A clear distinction should be made between effects on the individual and effects on the human race. The former result in sickness and death of exposed individuals; the latter are a threat to the future of mankind.

Effects on the individual. High doses of radiation cause sickness which may result in death; but, barring accidents, nuclear bomb tests will not cause exposures to such high doses. Low doses may result in cancer, often after many years of apparent well-being. The main types of cancer which may be expected are leukæmia and bone cancer, the latter in particular through accumulation of strontium-90 in bones. For animals, there is also convincing evidence that low doses of radiation shorten life-span without obvious disease. Whether this is true also for the human species is still under debate; it certainly is necessary to keep the possibility in mind.

Genetical effects. These occur in the form of gene mutations, and result in hereditary changes. There is no recovery from mutation. Once a mutation has occurred, there is only one way by which mankind can get rid of it: death or sterility of the individuals carrying the mutated gene. Mutations may be good, neutral or harmful in their effects; but in any species which, through long periods of natural selection, has become endowed with a well-working assembly of genes, the vast majority of mutations are harmful. For reasons which cannot be discussed here, even high doses of radiation are not likely to result immediately in the birth of malformed or otherwise obviously handicapped children, except when a pregnant woman is exposed. But any increase in the number of mutations is bound eventually to increase the number of such abnormal children, even though their occurrence may be spread over centuries. In addition, there will be a similar increase in the number of less-drastic hereditary changes, and these will swell the proportion of chronically ailing, emotionally unstable, mentally dull or otherwise sub-standard types in the human race.

The Threshold Concept

There is full consensus among scientists that radiation produces harmful effects on the exposed individual as well as on the human race as a whole; but opinions differ as to the magnitude of the damage expected from nuclear bomb tests. This is not surprising in view of the difficulty of obtaining pertinent data for human beings and the uncertainty factor involved in extrapolation from animal data. Questions directed in the House to the Prime Minister have shown that some Members of Parliament are aware of the key position which the threshold concept holds in all attempts to assess radiation damage quantitatively. Mr. Aneurin Bevan stressed the point that organisms differ in their sensitivity to radiation. This is true, but it is not relevant to the question whether or not there is a lower threshold to certain types of radiation damage. Whether or not there is such a threshold, individuals, organs and cells may and do differ in their sensitivity to radiation; but where a threshold exists, doses below a certain level of exposure—which may not be exactly the same for every individual, organ or cell—are entirely ineffective. Given the right amount of information, one can therefore determine a safe level of exposure below which no damage is to be expected. Where there is no threshold, no such safe level exists, and even the lowest exposure will produce damage in proportion to its magnitude.

There is very good evidence for affirming that there is no lower threshold for the production of mutations by radiation. In view of misleading articles in the daily Press, I want to emphasize that this conclusion is not invalidated by very recent experiments on mice, which indicate that the genetical effectiveness of radiation in certain types of cell depends on the time over which a given dose of radiation is spread. Estimates of the actual amount of genetical damage involve so many assumptions that they cannot be more than very rough approximations. For the case that bomb testing continues at the present rate, Prof. Pauling estimates that in about a hundred years, when equilibrium has been reached, about 15,000 seriously defective children will be born each year as the result of the tests. This value is within the wider limits of 1,000–40,000 adopted by the United Nations Committee. It does not include abortions, miscarriages, stillbirths and many minor hereditary defects which will have been produced at the same time. Nor does it take account of carbon-14 which, because of its very slow rate of decay, continues to produce radiation damage over many thousands of years. According to Pauling, already the bomb tests carried out so far "will ultimately produce about 1 million seriously defective children and about 2 million embryonic and neonatal deaths, and will cause many millions of people to suffer from minor hereditary defects".

There is as yet no evidence available which would allow a decision as to whether or not there is a lower threshold to the production of cancer, leukæmia and, perhaps, premature ageing by radiation. Recognizing this, the United Nations Committee has made all its calculations concerning these effects in duplicate: once on the assumption that a threshold exists, and a second time on the assumption that it does not exist. In the first case, as in that of mutation, even the lowest additional amount of radiation is dangerous in proportion to its magnitude; in the second, it seems likely that the present amount of fall-out is still below the danger level.

It should, however, be evident that in a matter like this—a matter of life and death for hundreds of thousands—one should act on the basis of the more pessimistic view until convincing evidence for the more optimistic one has been furnished. This seems also the opinion of the Medical Research Council. In its 1958 statement it writes: "In our view, it is not possible at this present time to decide whether there is or is not a threshold dose concerned in the induction of leukæmia and cancer, and the only scientific attitude to the problem at present is one of suspended judgment. Nevertheless, the significance of the alternative points of view in determining the ultimate assessment of risk should be clearly understood so that those who have the responsibility for acting on such assessments should be fully aware of the alternative possibilities that need to be taken into account".

The Role of Strontium

Strontium, as has been pointed out, plays a special part as a potential cause of bone cancer. It is therefore very disturbing to learn that the amount of this element in the rainfall over the United Kingdom has doubled during the past year. It is difficult to understand why this seems to cause little anxiety to the Prime Minister and his advisers. The amount of strontium-90 in the bones is measured in strontium units (1 strontium unit (S.U.) = 1 micromicrocurie of strontium-90 per gram of calcium). 1,000 S.U. is the industrially permissible dose; but in 1956 the Medical Research Council recommended that in a population with many growing children the allowable dose should not exceed an average of 100 S.U. and "that immediate consideration would be required if the level in the general population showed signs of rising greatly above 10 S.U.". The United Nations Report of 1958 presents figures which show that at the end of 1957 the average bone content of strontium-90 was 2·3 S.U. in countries with a milk-type diet and 14 S.U. in plant-eating communities, in both cases as the average over the next 70 years. This was before the spectacular increase of strontium-90 in rainfall, and although—as pointed out above—the relation between strontium in rainfall and strontium in the bones is complex, it cannot be doubted that this increase in fall-out will be reflected in a marked increase in the strontium-90 content of bones. If there has been a similar increase of strontium-90 fall-out in other parts of the world, the strontium content of the bones in some plant-eating peoples may already be well in excess of 10 S.U.

In regard to the future, the United Nations Committee estimated in 1958 that, if bomb tests continue at the same rate as between 1954 and 1958, the content of strontium-90 in the bones of people living about a hundred years hence will be 40 S.U. for countries with a milk-type diet and 240 for countries with a plant diet. Such figures, according to the Medical Research Council report, would certainly call for immediate consideration. Since the recent rise in strontium-90 fall-out has been so unexpectedly high, this situation may arise in a much shorter time.

Background Radiation

The Prime Minister seems to think it a cause for complacency that the human race has survived in spite of a considerable amount of radiation from natural sources. The opposite is true. It is highly probable that natural radiation causes many cases of leukæmia and bone cancer. There is nothing we can do about it. We just have to put up with it, as we have to put up with earthquakes and hurricanes. But the fact that many people are killed through such natural catastrophes does not make us complacent about death-rates from industrial accidents or careless driving. The fact that there is this inescapable amount of natural radiation, and that recently there has been added to it probably more than an equal amount of medical radiation, makes it even more imperative to keep radiation from any additional sources as low as possible.

For the genetical effects of radiation the situation is somewhat more complex and cannot be discussed here in detail. Only so much can be stated: mutations are the ultimate raw material for natural selection. Without mutation, there would have been no evolution. Naturally occurring mutations, too, are usually harmful, but Nature—in contrast to man—can afford to waste thousands of ill-adapted individuals for the sake of a single better adapted one. It is probable that in the course of evolution every species establishes a balance between the frequency with which its genes mutate and the amount of natural selection to which it is exposed. It is also probable that for mankind this balance has already been upset through the relaxation of natural selection, and that the frequency of even natural mutation may be rather higher than is desirable. Any additional mutations will shift the balance even further in the direction of genetical deterioration.

Manufacture of Nuclear Devices by Private Firms

I should like to make one final point. Prior to the discussion of radioactivity in the House of Commons on April 28, the Prime Minister was asked a question regarding safety measures in private firms which produce nuclear devices. The Prime Minister answered that the Atomic Energy Authority exercized the same sort of control and supervision in these firms as in its own establishments doing similar work. No doubt this is true; but there is a different angle to this question. The industrially permissible dose has been lowered repeatedly, and at present is only 1/14 of what it was in 1934. Yet it is still fairly high, and, if received in full by many employees for many years, would be a cause for concern, especially to geneticists. It is, however, asserted that very few workers in Government plants receive anything like this dose. In 1957, Prof. H. J. Muller, the leading expert on the genetical effects of radiation, pointed out that in private firms "the pressure of costs will tend to prevent the observance of more rigorous standards than those officially recognized, and there is therefore a danger of considerable radiation being received from the so-called peaceful atom, unless we further lower the ceiling". It would seem that in the United Kingdom we are reaching the stage where such a lowering of the officially permissible dose for employees in nuclear establishments should be taken into serious consideration.

C. AUERBACH

[1] Medical Research Council. The Hazards to Man of Nuclear and Allied Radiations. (Cmnd. 9780.) Pp. vii+128. (London: H.M. Stationery Office, 1956.) 5*s*. 6*d*. net. See *Nature*, **178**, 453 (1956).

[2] National Academy of Sciences–National Research Council. The Biological Effects of Atomic Radiation: a Report to the Public from a Study by the National Academy of Sciences. Pp. ii+40. The Biological Effects of Radiation: Summary Reports from a Study by the National Academy of Sciences. Pp. xiv+108. (Washington, D.C.: National Academy of Sciences–National Research Council, 1956.)

[3] Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. (General Assembly—Official Records: Thirteenth Session, Supplement No. 17 (A/3838).) Pp. iii+228. (New York: United Nations; London: H.M. Stationery Office, 1958.) 2.50 dollars; 18*s*.; 10.50 Swiss francs. See *Nature*, **182**, 1543 (1958).

[4] Medical Research Council. Statement on the Report of the United Nations Scientific Committee on the Effects of Atomic Radiation. Pp. 15. (Cmnd. 508.) (London: H.M. Stationery Office, 1958.) 1*s*. net. See *Nature*, **182**, 1543 (1958).

OBITUARIES

Dr. Jesse P. Greenstein

BIOCHEMISTRY and cancer research lost one of its leading figures with the sudden death on February 12 of Jesse Phillip Greenstein. He had been chief of the Laboratory of Biochemistry at the National Cancer Institute, Bethesda, Maryland, since 1946 and held this position at his death.

Born in New York in 1902, he graduated first from the Polytechnic Institute of Brooklyn in 1926 and then took an M.S. and finally Ph.D. in biochemistry at Brown University. In the next two years he held fellowships at Harvard (Prof. E. J. Cohn) and at the Kaiser-Wilhelm Institute, Dresden (Prof. M. Bergmann). This one year spent with Bergmann in Germany confirmed Greenstein's interest in amino-acids and settled much of the pattern of his future researches. Two valued reference books he always kept to hand on his desk were the collected works of Emil Fischer and of Max Bergmann. He returned to Harvard and during 1933–39 was instructor in biochemistry at Harvard College, and a research associate of Harvard Medical School. His research interests in this period were concerned with peptide synthesis, the physico-chemical characteristics of peptides in solution and the role of sulphydryl groups in protein structure and denaturation. Much of this work was of a new and fundamental nature and has retained a permanent place in the literature.

Leaving this special field of research, Greenstein entered the second and major phase of his career when in 1939 he moved to join the staff at the National Cancer Institute. He extended his earlier interests to include nucleoproteins and nucleic acids, and then with a team of workers devoted his energies to a survey of the enzyme spectra of living cells, normal and neoplastic. Greenstein's activities in this field undoubtedly stimulated the post-war surge of research into the chemistry of growth. With his colleagues he published more than a hundred papers in the period 1940–47 dealing with this problem. Much of this work was incorporated in his first book published in 1947, "Biochemistry of Cancer". This book has remained the most important and most quoted survey of experimental cancer research. It was revised and of necessity greatly extended in its second edition in 1954 and is unlikely to decrease in value for many years to come.

While retaining an interest in enzymology, Greenstein turned his interest back to amino-acid chemistry. Papers published over the period 1948–58 describe the use of enzymatic methods for the resolution of amino-acids. Making use particularly of a kidney enzyme, designated 'acylase', Greenstein and his colleagues showed that by asymmetric hydrolysis of acyl-DL-amino acids both the pure L- and D-forms could be obtained in good yield and of high optical purity. During the past three years the application of these pure isomers in nutritional and metabolic experiments was being studied.

The volume of published work conveys some idea of Greenstein's immense energy. The carpeted office approached through a protective screen of secretaries was not for him. Instead, there was an open door and a pair of hands ready, indeed anxious, to help with practical work and a fund of advice and experience. He was always anxious to help along the younger workers of his group and would always give them full credit for any achievements. He also afforded a very generous welcome to workers from many countries, and the hospitality of his family, as well as of the laboratories, must have left them with a very happy impression of American life.

Greenstein himself went outside the United States on two occasions only—to a conference at the Papal Academy in Vatican City in 1949, and to Japan in 1956. He did, however, take a very prominent part in American scientific affairs. He was, for example, a past chairman of the Division of Biological Chemistry of the American Chemical Society and a member of the National Research Council's Committee on Biochemistry. He was on the editorial boards of *Cancer Research* and *Archives of Biochemistry and Biophysics*, while in recent years he was joint-editor with Prof. A. Haddow of "Advances in Cancer Research". At the time of his death he was just completing a major treatise on amino-acid chemistry. Among many formal acknowledgments of his work were included a Distinguished Service Award from the U.S. Government (1954) and the Hillebrand Prize of the American Chemical Society (1957).

Though modest about his own contribution, he was visibly proud of the work of his section, of his country and above all of his family. He will be greatly missed and all will sympathize with those near to him at their loss.

Douglas Hamer

Dr. Greenstein's contributions extended widely in the fields of amino-acid, peptide and protein chemistry, and of nutrition. In the past few years he had devoted much effort to the elaboration of a completely soluble diet composed of chemically defined constituents; and at the time of his death he was engaged (with M. Winitz), in the final stages of a major work on the chemistry of the amino-acids, which is to appear in three volumes, of which the first is now in the press. But apart from these, his contributions to cancer research alone would have more than sufficed to establish him among the leading biochemists of his time. He was an accomplished writer, and his "Biochemistry of Cancer" had, and has, immense influence, and proved a very significant stimulus to the subject as a whole.

Of his own work, two aspects were of particular importance; first, his studies of the mechanism of production—and the significance—of the dramatic decline in liver catalase activity which is observed in tumour-bearing animals; and secondly, his analysis and comparison of the distribution and activity of a host of enzyme systems in normal and cancer cells. In spite of the extreme difficulty and complexity of these problems, there gradually emerged a real and satisfying conclusion, namely, that although tumours mostly possess the same enzymes as do normal tissues, qualitatively, none the less they tend, enzymatically, to converge to a common type, and hence show more resemblance to one another biochemically than to the normal tissues from which they arose.

All these, and many other contributions, embodied in upwards of 250 papers, brought him international acclaim. But we shall also remember him for his human qualities, and his combination of serious devotion with much courage and humour. Certainly I have good cause to be grateful for many years of happy association with him; and Bethesda without him can never be quite the same. All who admired him will be glad to know that there has now been established, in his remembrance, a Jesse P. Greenstein Memorial Foundation, to be administered by a small committee of his colleagues, and which will, in cases where it is necessary or helpful, provide tuition and support during the years of undergraduate study in the arts or sciences, "to the son or daughter of a scientist who has made notable contributions to the medical, physical or biological sciences, and who is deceased".

Alex. Haddow

Dr. Arthur Walton

Dr. Arthur Walton, who died suddenly in Cambridge on April 6, was best known for his pioneering research in the field of sperm physiology and artificial insemination of farm animals. He was born in London, on March 16, 1897, of Scottish parents, and educated in Edinburgh, first at Daniel Stewart's College and later at the University, where he obtained in 1923 the degree of bachelor of science (agriculture). It was also in Edinburgh, at the Animal Breeding Research Department, where he received his early training in research methods and published, in 1924, his first paper, on "The Flocculation of Sperm Suspensions in Relation to Surface Charge". Keen interest in sperm physiology prompted Walton to move to Cambridge and take up research on animal reproduction. In 1926 appeared his first communication in *Nature*, on "Preservation of Mammalian Spermatozoa", a subject which he expanded in the following year in his Ph.D. dissertation, and to which he devoted his special attention throughout his scientific life.

Among Walton's most outstanding contributions to the subject of sperm physiology was the first demonstration that ram semen, properly collected and stored, can be sent on long journeys to distant countries, to be used there for successful insemination of ewes; next, there were the experiments which proved that 'cold shock' can destroy the fertilizing ability of bull and ram spermatozoa. Of great scientific significance was his observation that the metabolic activity of ram and bull spermatozoa, particularly their respiration, is directly correlated with motility; and the discovery that respiring spermatozoa produce under certain conditions hydrogen peroxide which, in turn, is responsible for a gradually developing inhibitory effect on respiration and a decline in sperm motility. During his more recent investigations, Walton developed a novel and ingenious method of maintaining sperm alive for long periods, in a perfusion apparatus where nutrient substrates are fed continuously to a sample of semen and the toxic metabolites removed at the same time.

In addition to the work on spermatozoa, Walton has been keenly interested in various other aspects of reproductive physiology, including mating behaviour in animals and female fertility. He was the first to make detailed observations on ovulation in the rabbit, and to study the effect of maternal influences on the size of offspring in reciprocal crosses between large and small breeds of horses.

As a member of the University School of Agriculture and the scientific staff of the Agricultural Research Council, Walton spent nearly thirty years of his life in Cambridge, much of it in his laboratory at the Animal Research Station, in close association with many young research workers, always ready to help, to guide, and to advise. Although primarily concerned with physiological problems, Walton had also a profound knowledge in the field of general biology and agriculture. His contributions to agriculture, especially those which led to the establishment of the practice of artificial insemination in farm animals, were recognized in 1957, by the award of the Medal "for outstanding research in agriculture" from the Royal Agricultural Society of England. Walton's many friends all over the world will mourn the untimely death of this outstanding scientific worker.

J. HAMMOND
T. MANN

Dr. F. Tattersfield, O.B.E.

DR. FREDERICK TATTERSFIELD died at his home in Harpenden on May 1 at the age of seventy-eight. He may well be described as the founder of modern research on insecticides.

Dr. Tattersfield was born near Dewsbury in Yorkshire and went to Dewsbury Grammar School and the University of Leeds. From Leeds he graduated in chemistry with first-class honours. His first job was in association with the Leeds City Analyst, where for a number of years his work ranged over all the typical activities in such a department. In 1908 he joined a paint manufacturing firm; here his work was chiefly concerned with research on anti-fouling paints for ships.

Dr. Tattersfield went to France in the First World War as a founder member of the Friends' Ambulance Unit. He was invalided out in 1917, and went to Rothamsted Experimental Station, where he remained for the rest of his working life. He originally had a temporary appointment in the Chemistry Department, but he soon founded the present Department of Insecticides and Fungicides, of which he was the head for twenty-nine years.

Dr. Tattersfield's earliest work was concerned with the control of soil pests and he carried out some work on the structure – toxicity relationships of chemicals to wireworms. He also studied the factors influencing the decomposition of naphthalene in the soil and the effect of different rates of decomposition on its insecticidal action. He then proceeded to study the effect of a range of chemicals on the insects that attack the aerial parts of the plant, again attempting, so far as possible, to relate toxicity with structure in some systematic way. In the course of this work he discovered the outstanding ovicidal properties of dinitro-*o*-cresol, a substance which has been used as a winter wash for fruit trees ever since. At that time chemical manufacturers had little confidence in the development of effective synthetic organic chemicals for pest control, and Dr. Tattersfield in his search for highly biologically active chemicals turned his attention to plants. He examined a wide variety of plants for insecticidal activity, but his main work was done on the fish poison group, particularly *Derris* spp. and *Tephrosia* spp. and on *Pyrethrum*. His contributions on the isolation of the active principles of these plant products, the assessment of their insecticidal activity and their chemical estimation were quite outstanding. He studied many phases of the production and assay of pyrethrum as an insecticide and played a large part in the founding of the Kenya pyrethrum industry, an industry which has proved of the greatest value to the economy of the country.

During the course of his work, Dr. Tattersfield evolved precise methods of administering doses of chemicals to insects and introduced statistical procedures for the quantitative assessment of results.

The mere cataloguing of Dr. Tattersfield's contributions to knowledge on insecticides, substantial though they are, gives a very inadequate idea of what the subject owes to his influence which, fortunately, was widely felt owing to his high international reputation. When he entered the subject the standard of work was very low and no serious attempt was being made to obtain reproducible quantitative results of known significance. Dr. Tattersfield insisted on the importance of precise quantitative data where the factors known to influence the results were standardized, so far as possible, and where both the design of the experiment and the results would satisfy accepted statistical criteria. In doing this he set standards which, over the course of years, have been accepted to the inestimable benefit of the subject.

Dr. Tattersfield was always a source of inspiration to his colleagues, to whom he was unfailingly kind and helpful. His justly acquired high reputation never changed his modest and unassuming personality, and his death will leave many of us with a deep sense of personal loss. He leaves a widow and one son.

C. POTTER

Dr. G. K. Groetzinger

DR. GERHART K. GROETZINGER, a principal scientist at the RIAS Division of the Martin Company, Baltimore, died on March 30 at the age of fifty-one. Born in Vienna, Austria, he received his doctorate in physics from the University of Vienna in 1931 and was a member of the faculty there before going to the United States in 1938.

Dr. Groetzinger has been associated as a faculty member, research worker and consultant with the University of Illinois, Ohio State University, the Enrico Fermi Institute for Nuclear Studies at the University of Chicago, the Lewis Laboratory of the National Advisory Committee on Aeronautics, and the Los Alamos Laboratory of the Atomic Energy Commission. Dr. Groetzinger joined RIAS in January 1956, and his work there since then had dealt primarily with solid state physics and cosmic-ray experiments performed in Earth satellites and high-altitude balloons. His work included some of the pioneer investigations of such fields as magneto-photoelectric effects in semi-conductors and the nuclear interactions of mu mesons.

Mr. H. Curtis

MR. H. CURTIS, production director of Leda Chemicals, Ltd., died on May 20 at the early age of thirty-nine.

Mr. Curtis graduated with honours at the Manchester College of Technology in 1941 in chemical engineering. After working during the War with chemical firms, he went to Sondes Place Research Institute in 1948 and in 1950 to Leda Chemicals, Ltd. He was appointed as a chemical engineer at a time when the firm was starting to manufacture fine chemicals. During his service with the firm, Mr. Curtis designed and constructed plant for the manufacture of quaternary ammonium compounds, cyanamide monomer and a range of other fine chemicals, notably rubber chemicals such as alkyl dithiocarbamates.

During the year 1953–54 Mr. Curtis went to Israel and worked on process development with Israel Mining Industries, Ltd. On returning he was elected a director of Leda Chemicals and its associated companies, Cunningham Smith, Ltd., and Lea Valley Chemicals, Ltd., becoming responsible for production and chemical engineering in these companies.

NEWS and VIEWS

Mechanical Engineering at Belfast : Prof. F. V. Warnock, O.B.E.

Prof. Frederick Victor Warnock will retire on September 30 from the chair of mechanical engineering at The Queen's University of Belfast. He received his engineering education at the Royal College of Science, Dublin, and has been a member of the Faculty of Applied Science and Technology at Belfast since its inception in 1921. He is now the sole surviving founder member. He was the first occupant of the chair of mechanical engineering, founded in 1955, though he had served as head of the Department in the Belfast College of Technology and as extra-mural professor in the University since 1938. Many of his former students hold positions of responsibility in universities, industry and research organizations, and they would all testify to his skill as a teacher. A wider public is familiar with his clarity of exposition through his book on "Strength of Materials".

In his long academic career at The Queen's University, Prof. Warnock has been actively concerned in the most successful collaboration between the University and the College of Technology, and as professor and dean of the Faculty, has been responsible for the planning of the new engineering building which will serve the needs of both bodies for advanced engineering studies. His main research interest lay in the shock properties of metals and, though he published a number of papers in the *Proceedings* of the Institution of Mechanical Engineers and of the Iron and Steel Institute, these do not reveal the full importance of his work. During the Second World War he was responsible for some experiments in shock testing of steels on behalf of the Admiralty, and these results have never been published. Much important work has been done on repeated impact testing in other universities by men who learned their techniques and received their inspiration from Prof. Warnock.

The Editors regret the delay in publishing this issue of "Nature". From now on, every effort will be made to bring out succeeding issues as quickly as possible until the normal date of publication is resumed

Dr. B. Crossland

The appointment of Dr. B. Crossland to the chair of mechanical engineering at The Queen's University, Belfast, in succession to Prof. Warnock, has recently been announced. Dr. Crossland was educated at Simon Langton's Grammar School, Canterbury, and Nottingham University College, where he took a London honours degree in 1943. He obtained his practical experience with Rolls-Royce, Ltd., Derby, first as an apprentice and then as technical assistant in the experimental vibrations section which dealt with both reciprocating and the then novel gas turbine engines. After a brief period as a lecturer at Luton Technical College he was appointed to the staff of the Mechanical Engineering Department, University of Bristol, where in 1957 he was promoted to senior lecturer.

In 1947 Dr. Crossland obtained the degree of M.Sc. for a thesis on the "Axial Vibration of Crankshafts" and in 1954 the Ph.D. degree for a thesis on "The Effect of Fluid Pressure on the Shear Properties of Materials". These theses reflect a gradually changing preoccupation from problems in the field of vibrations and machines to those concerned with strength of materials, in particular plasticity and fatigue. To these latter subjects he has, in recent years, made important contributions; for example, in elucidating the effect of hydrostatic pressure on brittle materials, in determining the behaviour of thick tubes subjected to internal pressure, and in investigating the behaviour in relation to fatigue of materials subjected to cyclically varying triaxial stresses.

Automatic Programming of Digital Computers

The first national conference devoted to problems of automatic programming of digital computers was held during April 1–3 at Brighton Technical College. Organized by the Mathematics Department, the conference was attended by 111 representatives of computer manufacturers, research establishments, industry, universities and technical colleges. The conference recommended that Brighton Technical College be asked to establish, with the help of the profits of the conference and the assistance of computer manufacturers, a national information centre on auto-programming. The aim of this centre would be to collect a comprehensive library of documents on the subject, to make available to subscribers, by a postal service and otherwise, copies of any such document required, and to publish, from time to time, in the British Computer Society's *Bulletin*, lists of new documents acquired. It was also suggested that the British Computer Society be asked to co-opt on to its sub-committee concerned with problems of a universal autocode a representative of the Brighton Technical College, as organizers of the conference. A list of definitions of commonly used terms, such as 'interpretive routine', 'translation routine', 'compiler', 'generator', etc., suggested in a paper by Dr. Stanley Gill, was circulated to the participants for comment. This list is also to be published in the Computer Society's *Bulletin* so that any member of the Society who was not at the conference may take part. The proceedings of the conference are to be published by the Pergamon Press.

British Association of Corrosion Engineers

The British Association of Corrosion Engineers was formed at a luncheon given under the auspices of *The Corrosion Engineer* on May 29. The objects of the Association will be generally to promote the dissemination of technical information about corrosion matters and to develop by means of social activities the free interchange of information among members. In due course the Association, which is, of course, essentially non-profit making, will progress towards the establishment and acceptance of suitable qualifications for corrosion engineers, and the promotion of standardization in the terminology and techniques of corrosion control. When the Association is in full operation it is intended to hold full-scale meetings with papers, films and discussions, which should be of great benefit to the corrosion engineering profession as a whole and which will promote and foster its growth and development as well as being of general service to industry. Further information can be obtained from the Hon. Secretary, British Association of Corrosion Engineers, 97 Old Brompton Road, London, S.W.7.

The Average Length of Working Life

FIGURES showing the average expectation of working life for males in Great Britain, which have been prepared by the Ministry of Labour and National Service, are set out in a booklet called "The Length of Working Life of Males in Great Britain" (pp. 24. London: H.M. Stationery Office, 1959. 3*s*. 6*d*. net). The publication contains tables and charts which are designed to provide answers to questions like: How many years on the average can men of a given age expect to continue at work? What proportion of the men of a given age in the working population can expect to be still working at sixty-five and then have a period of retirement? What were the estimated losses from the working population in 1955 owing to death and retirements? For example, the 1955 table shows that on the average boys aged fifteen can expect to have 48·4 years in the working population. Of the men aged thirty in the working population, 62 per cent can expect to be still in the working population at age sixty-five. For those men aged sixty-five in the working population, 75 per cent can expect to retire at some later age. A very large population (31 per cent) can expect to retire before reaching their sixty-sixth birthday. A comparison between 1931 and 1955 shows that over this period the expectation of working life at birth rose from 40·6 years—an increase of 12½ per cent. This was entirely due to the reduction in mortality-rates, which outweighed the effect of the raising of the school-leaving age and of the movement to earlier retirement. There is a growing demand for the kind of information given in these tables because private pension schemes and the new social security legislation introduced into Britain during the present century have made it possible for an increasing number of people to spend a significant number of years in retirement. 'Probability of survival' tables have been in use for a long time, but since there is now a substantial difference at particular years of age between the average expectation of life and the average expectation of remaining in the working population, separate tables show the expectation of working life.

Training for Skill

"Training for Skill", by Lady Gertrude Williams, issued as No. 205 in the Fabian Research Series (pp. 28. London: Fabian Society, 1959. 2*s*.), is based on the factual information regarding boy apprentices collected in a survey, "Recruitment to Skilled Trades" (see *Nature*, 181, 373; 1958). It also covers the Carr report, "Training for Skill", which is criticized for failing to face the profound changes in industrial structure and in public education which have made many of the traditional methods inappropriate to present needs, although the report contains an agreed criticism of the inflexibility of the present regulations. The pamphlet urges that some new method must be found which ensures that an adequate supply of training vacancies is available to provide enough skilled workers for future needs, and that the costs of training are spread more justly over all the firms that benefit from the employment of adult skilled men. It should also ensure that men capable of learning to do a job are not permanently excluded simply because they missed the opportunity to train when they were sixteen years old, that the quality of teaching in the workshops is improved, and that the theoretical instruction is graded to suit the capacities of the pupil. Lady Williams refers to some schemes for group training recently instituted and an extension of the 'sandwich system' as possibilities to be explored, and also suggests that apprenticeship might come to be regarded more definitely as a function of education rather than of industry. In an introduction in which she discusses industry's present needs and the limits of mass production, Lady Williams stresses the real danger that there will not be sufficient skilled workers available to understand and execute the instructions of the increased number of scientific advisers and technologists in industry.

Technics and Purpose

Two additional booklets have been announced in the admirable series launched to examine the issues arising out of the growing importance of scientific techniques in society, the rapid expansion of technological and other education and the purposes and values involved in the light of the Christian faith. The first (On Being a Technologist. Technics and Purpose, No. 5. Pp. 33. S.C.M. Press, Ltd., London, 1959. 2*s*. 6*d*. net), by Prof. D. G. Christopherson (Imperial College of Science and Technology, London), suggests that, contrary to all the pessimistic views of the persuasive advocates of 'Admass', the total responsibility shared by the members of an industrial society has increased. Once this belief is accepted it calls for a large extension of the attitude of mind formerly associated with the professions; many more people will have to make judgments based on knowledge and reason. Such a society will become increasingly individual and less amenable to the techniques of mass suggestions.

The second (The Educated Man Today and Tomorrow. Technics and Purpose, No. 6. Pp. 26. S.C.M. Press, Ltd., London, 1959. 2*s*. 6*d*. net), by Sir John Wolfenden, is noteworthy not only because it paints a clear picture of an educated man but also because it does so without becoming trite, or condescending. Besides those qualities of character which are the hallmarks of education, Sir John believes that the educated man will accept his place in the world of Nature and will see that he understands what the scientists and technologists are doing, the nature of their thinking, and, as their numbers and influence are continually increasing, the way in which they should be educated. The third requisite for an educated man put forward by Sir John shows a remarkable likeness to that advocated by Prof. Christopherson, albeit arrived at from a different approach. Prof. Christopherson writes, "Somehow or other, if a man is to do a proper job he must find means of continuing the process of education through his whole professional life, and the need to do so is in itself a stimulant to thought not only about the immediate problems of the profession but about the deeper problems of purpose, proportion and responsibility". For Wolfenden, "the restlessness of the human mind is a divine restlessness; and however solid these brick walls may seem to be, it is part of man's nature that he cannot resist banging his head against them. For it is not in the problems of our relations with other human beings or of our relations with the world of Nature that the ultimate problem lies; it lies in our relations with what is neither of these. What is very clear is that an education with this basis will not end at school-leaving age, or with the acquisition of a university degree. There is no reason to suppose that it ends with the grave".

Electrotechnology in Australia

The annual report for 1957–58 of the Division of Electrotechnology of the Commonwealth Scientific and Industrial Research Organization of Australia describes the three main activities of the Division: the maintenance of the Commonwealth standards of measurement of electrical quantities, including the standard of frequency; calibration of electrical and magnetic instruments; and research on the improvement and extension of the electrical measuring and standards facilities and on the dielectric properties of insulating materials and the microwave spectra of gases. New apparatus installed includes a small vacuum evaporation plant; a calculable capacitor and associated measuring equipment; and facilities for making impedance and other measurements at microwave frequencies chiefly within the 9,000 Mc./s. range. The hyperfine structure of the microwave spectra of heavy-water molecules is being analysed on the high-speed digital computer *Silliac* to determine more accurately the electric field gradient at the position of the deuteron nuclei in these molecules and to estimate the magnetic constants governing the smaller effects observed in the spectra. Special furnaces have been constructed to assist in the determination of the conditions required for the successful growth of large single crystals of organic materials, and the study of the dielectric properties of polycrystalline materials and liquids has been extended. Both experimental and theoretical work has been carried out on dielectric breakdown in the alkali halides and a theoretical study based on the harmonic motion of the interacting electron–lattice system has been made of the superconducting specific heat and transition temperature of multivalent metals.

Wool Industries Research Association

The report of Dr. A. B. P. Cassie, director of research of the Wool Industries Research Association, presented to the annual general meeting of the Association on April 7, includes, besides details of the membership of the Council and Committees and a list of staff, a bibliography of publications in 1958, including lectures given by members of the staff, patents and some forthcoming publications (Wool Industries Research Association, Report of the Director of Research for 1958. Pp. 35. (Publication No. 212.) Headingley, Leeds: 1959). Modifications have been made to the pilot scouring plant, while methods for determining oil and grease in scoured wool and tops have been extensively investigated. Further work on the pulling of rags has confirmed that there is little, if any, difference in the quality of the yarns or fabrics prepared from the differently treated yarns. The work on examining the state of a yarn at the instant of break during spinning is now almost complete, and a technique has been evolved for determining whether the fibres slip or break when the yarn breaks for use with 'Fibro' but not for wool. Further experience with wool/'Terylene' blends indicates that there can be no guarantee against the tight ends or 'fiddle-string' fault developing, as procedures which are entirely satisfactory with all-wool yarns can give rise to snatch and stretching of wool/'Terylene' yarns without breakdown, but a procedure which seems to provide reasonable protection during cone-winding is indicated. The review of milling was expanded and work continued on the scouring of wool/'Terylene' worsted cloths. The study of damage to wool in dyeing was extended to coarse wool, and work was restarted on the efficacy of dieldrin in moth-proofing. The first part of the work on the examination of the washing process of wool by microscopical methods was completed, and determinations of the latent heat of sublimation of nitrogen-substituted amides, which contain a peptide group similar to that in keratin, suggest that the strength of this bond is 4–5 kcal. Homogenous membranes are now being used to study the effects of organic solvents on the rate of diffusion of dyes into keratin.

East Africa High Commission: Report for 1958

Approximately half the illustrated and very readable annual report for 1958, of the East Africa High Commission (pp. iv+92. Nairobi: Government Printer, 1949. 5*s*.) is concerned with research and scientific services, including some material to be found in "Colonial Research, 1957–58" and in the annual report of the East African Industrial Research Board as well as in "The Colonial Territories, 1957–58". Although more limited territorially, it has a somewhat more popular appeal and is well designed to show the important contribution which scientific research is making to development and welfare in East Africa. This is particularly true of the work of the East African Agriculture and Forestry Research Organization, the Veterinary Research Organization, the Fishery Research Organization, the Marine Fisheries Research Organization, the Trypanosomiasis Research Organization, the Virus Research Institute and the Institute for Medical Research. Expenditure on research was £806,721 and on the Desert Locust Survey £438,982, but it is stated that for the past two years difficulty in recruiting suitable technical and scientific staff has been the main hindrance to the expansion programme.

Acta Biologica Cracoviensia

A new botanical journal, *Acta Biologica Cracoviensia* (Sér: Botanique) (1, No. 1; 1958), has been published for the Polish Academy of Sciences under the editorship of Mme. Prof. M. Skalinska (Cracovie. Inst. d'Anatomie et de Cytologie des Plantes; Rue Jana 20). The contents of this first issue are partly palæobotanical, partly cytological. An article on the interglacial flora in Ganovce travertines in Eastern Slovakia is contributed by V. Kneblova; and there are short descriptive accounts of the genus *Cunninghamia* in the European Miocene by W. Szafer and of *Salvinia* and *Azolla* from the same geological horizon in Poland by M. Lancucka-Srodoniowa. The several cytological investigations, by Prof. Skalinska and her colleagues or pupils, deal with the curious behaviour of nuclei in the anther tapetal layer in species of *Cucurbita*, *Aconitum* and *Valeriana*. Up to a certain point the tapetum consists of normal uninucleate cells, but about the time of the prophase of meiotic divisions in the pollen-mother-cells some unusual cytological developments are induced: while some of the tapetal cells and their nuclei remain as before, others may become polynucleate, and yet others may show more or less conspicuous enlargement and, by endomitosis, may give rise to nuclei of different size categories corresponding to 4*n*, 8*n*, and even 16*n* chromosomes complements. These developments, described by these authors as "the differentiation of the tapetal cells", are considered to result from successive stimuli which can be related to developmental changes in the developing pollen-mother-cells and the tetrads to which they give rise. On the evidence to date, based on species drawn from widely separated families, it appears that these seemingly anomalous developments in the tapetum may well prove to be of very general occurrence. The texts are in English throughout, with bilingual titles. The journal is well produced, with a good clear type, and is illustrated by line drawings and by photographic plates of good quality.

Link between the Annelids and the Arthropods ?

A NEWLY FOUND fossil from near the base of the Cambrian of South Australia shows affinities which may throw some light on the origin of the arthropods. The new form is described by M. F. Glaessner in the *Transactions of the Royal Society of South Australia* (81, 185; 1958) and has been named *Spriggina floundersi*. It represents a new family of the polychaete annelids. The body is flat, the head being without external segmentation and having lateral extensions giving it a roughly horseshoe shape, the trunk consisting of a very gently tapering series of segments with appendages terminating in bristles, numbering up to about 40 and not differentiated into a tail. The largest specimen measured 46 mm. long and 11 mm. wide. Since fossil jellyfish are found at the same locality it is not necessary to assume that *Spriggina* was hard-bodied. Certain features of the head resemble those of the living group Tomopteridae, members of which are pelagic. It is accordingly suggested that the aberrant pelagic adaptations of the Tomopteridae may conceal more primitive characters. In particular the lateral extensions of the head of *Tomopteris* and its composite nature may foreshadow the formation of primitive arthropod head shields such as those of the Middle Cambrian proarthropod (trilobitomorph) *Marrella*, and of trilobite larvæ or primitive trilobites. This possibility does not seem to have been considered by the zoologists.

The Fairy Fly

Prestwichia aquatica, the fairy fly, is a hymenopterous insect which parasitizes the eggs of aquatic insects, especially water-beetles, including *Dytiscus marginalis* L. It was first discovered by Sir John Lubbock in 1864 in a pond in Kent and was not seen again for thirty years, when Frederic Enock found a few specimens in a horse-pond. In 1896, and again in 1898, Enock records that he was able to find aquatic insect eggs containing both male and female specimens of *Prestwichia aquatica*, which eventually he reared. The eggs were taken from the previous year's stems of the water-plaintain, *Alisma plantago-aquatica* L. In a communication to the *Journal of the Quekett Microscopical Club* (28, No. 4; 1958), C. I. Ison writes that, since the work of Enock, *Prestwichia* has probably been found only on two occasions in Great Britain. The most recent was at Loughton, Essex, on July 17, 1958, when Ison saw two female fairy flies emerge from an unidentified egg. The males are much slower in emerging. Subsequent observations showed that twenty-six days elapsed before any movement of the parasites was noticed in the host egg after oviposition, and it was twenty-eight days before any females emerged. From one 2-mm. egg of the beetle, *Ilybius ater*, five male and twelve female fairy flies emerged. Observation of *Prestwichia aquatica* at the surface film of the water showed that they are quite at home whether they are above the film in the air or below, in the water, walking upside down.

Predatory Animals in Spain

DURING the past four years organized campaigns against predators have been taking place in Spain (*Oryx*, 5, No. 1; April 1959). Among the 100,000 mammals and birds killed were 36 martens, 1,051 wild cats, 55 lynxes, 380 badgers, 7,250 eagles and other birds of prey. Such indiscriminate slaughter can only lead to extermination of the rarer species, especially, for example, of the southern race of the Spanish lynx, which is chiefly a lowland animal. Both the imperial eagle and the short-toed eagle, which lays only one egg, nest in easily accessible places and are especially vulnerable. In Spain there is as yet little interest in the preservation of wild life, and the conservation laws are not enforced effectively. Every predator is believed to be an enemy. A new conservation law will remove both the lynx and the lammergeier from the list of vermin, and will give the lammergeier complete protection for five years.

Banana Wilt Investigations

IN extended investigations of the vascular wilt disease of bananas caused by *Fusarium oxysporum* f. *cubense*, R. H. Stover has examined the evidence for clonal differentiation among wild type isolates of the pathogen (*Canad. J. Bot.*, 37, No. 2; 1959). *F. oxysporum* f. *cubense* exists in diseased rhizomes and pseudostems of Gros Michel bananas in two major clonal groups, or cultivars, designated 'Odoratum' and 'Inodoratum', because of the presence or absence of a distinctive odour from cultures after 4–8 days on various media. Three clones of the 'Inodoratum' cultivar, which are difficult to distinguish morphologically on peptone dextrose agar, were, however, distinguishable by cultural interaction and pathogenicity tests in the field. Also, some clones of the 'Inodoratum' and 'Odoratum' cultivars have been shown to differ quantitatively in pathogenicity in the field. Clone *C* from Honduras, of limited distribution, induced the most rapid disease-spread and destruction of banana mats, followed by clone *E* from Panama. There was an association between the 'Inodoratum' and 'Odoratum' cultivars and the syndromes induced in Honduras: the former usually induced strong yellowing of erect leaves, whereas the latter usually induced leaf collapse at the petiole with little or no leaf yellowing.

Exhibition of Old-time Beekeeping

AN interesting exhibition of equipment used by old-time beekeepers in connexion with their ancient craft is open until the end of September at the

Museum of English Rural Life, Whiteknights Park, Reading. This, probably unique, collection of log hives, skeps of various materials and patterns, hackles, old style wooden hives of various kinds, honey and wax extractors, drone traps, feeders, smokers, queen excluders, etc., has been collected during the past few years by the Bee Research Association and is on permanent loan to the Museum. Entrance is free and a useful descriptive catalogue can be obtained from the Museum.

International Conference on Fishery Statistics

An international meeting of experts on fishery statistics in the North Atlantic area is to be held in Edinburgh during September 22–30. The conference is being convened by the Food and Agriculture Organization of the United Nations in co-operation with the International Commission for the North West Atlantic Fisheries and the International Council for the Exploration of the Sea. Governments concerned with the North Atlantic fisheries have been invited to nominate experts directly concerned with collecting, analysing and publishing statistics on the fishing industries and trades of their countries, and the Scottish Home Department will act as hosts to the delegates. It is hoped that delegates will be able to identify the main difficulties encountered in providing statistical data for the use of Governments, international agencies and the fishing industry, and will indicate the action to be taken to eliminate or reduce such difficulties.

The Marine Biological Association of India

The Marine Biological Association of India was founded at Mandapam Camp, to promote interest in marine biological and cognate sciences. The Association was formally inaugurated by the Hon. Mrs. Lourdhammal Simon, Minister for Fisheries and Local Administration, Madras State, on January 3. The following officers were elected: Dr. S. Jones (president), Prof. R. V. Seshaiya (vice-president), Dr. R. Raghu Prasad and Dr. C. P. Gnanamuthu (secretaries), Dr. R. P. Varma (assistant secretary), Shri K. V. Rao (treasurer), Dr. P. N. Ganapati (editor), Dr. R. Subrahmanyan (joint editor), and Dr. S. V. Job (managing editor). The official organ of the Association, the *Journal of the Marine Biological Association of India*, is expected to be issued half-yearly. Membership is open to all who are interested. All correspondence should be addressed to the Secretary, Marine Biological Association of India, Marine Fisheries P.O., Mandapam Camp, South India.

University News: North Staffordshire

The following appointments, among others, have been made: Mr. E. M. Hugh-Jones, fellow and tutor of Keble College, Oxford, professor of economics, in succession to Prof. B. R. Williams; Miss A. Eden, senior lecturer in education, Homerton College, Cambridge, lecturer in education and women's warden; Dr. V. C. Ewing, pressed steel research fellow, University of Oxford, lecturer in chemistry; M. F. Newman assistant lecturer in mathematics.

Announcements

An international conference on High Energy Accelerators and Instrumentation will be held at CERN during September 14–19. Further information can be obtained from the Conference Secretariat, CERN, Geneva 23, Switzerland.

The thirteenth congress of the International Scientific Film Association is to be held in London and Oxford during September 23–October 2, under the auspices of the British Scientific Film Association. Further particulars can be obtained from the Association's office at 3 Belgrave Square, London, S.W.1.

The International Council for Building Research, Studies and Documentation is organizing an international congress, to be held in Rotterdam during September 21–25. The topics for discussion include the design and calculation of structures; research problems relating to the application of heavy concrete elements; and fundamental aspects of the transmission of knowledge. Further information can be obtained from the C.I.B. Secretariat, c/o Bouwcentrum, P.O. Box 299, Rotterdam.

The Dublin and District Section of the Society of Chemical Industry, in conjunction with the Agriculture Group of the Society, is to hold a symposium in Dublin during September 15–18. The subject will be "Chemical Aspects of the Production and Use of Grass", and it is intended that the meeting shall include the presentation and discussion of pre-printed papers, and lectures and visits to places of scientific interest. Further information can be obtained from the honorary secretary, R. O. V. Lloyd, Chemist's Laboratory, A. Guinness Son and Co. (Dublin), Ltd., St. James's Gate, Dublin.

The Electrical Engineering Department of the University of Birmingham is arranging two informal residential conferences in September 1959. The first, on dielectric devices, will be held during September 14–17, and the second, on modern network theory, during September 21–24. Preliminary programmes of papers and discussions have already been arranged. Further information can be obtained from the Secretary of the Electrical Engineering Department, The University, Birmingham 15. In order to preserve the informal nature of the conferences, numbers will have to be strictly limited.

The fourth annual conference of the British Society for the Philosophy of Science will be held at Newnham College, Cambridge, during September 25–27, when the following papers will be read: "Scientific Research and the Philosophy of Science", by Prof. H. Dingle and Prof. H. C. Longuet-Higgins; "Classification, Concept-formation, and Language" by Miss M. Masterman and Dr. A. Koslow; "Knowing and Being", by Prof. M. Polanyi and Prof. R. B. Braithwaite; "Biology and Physics", by Prof. J. H. Woodger and Dr. E. H. Hutten. Further information can be obtained from the honorary secretary of the Society, Miss M. B. Hesse, University College, London, W.C.1.

The first Congrès International de Prophylaxie Criminelle will be held in Paris during September 27–30. Further information can be obtained from M. Stanciu, 7 Avenue Général Leclercq, Boulogne sur Seine.

Erratum. In the communication entitled "Possible Causes of Geomagnetic Fluctuations having a 6-Sec. Period", by H. J. Duffus, J. A. Shand and Sir Charles Wright, published in *Nature* of May 23, p. 1479, the caption for Fig. 3 should conclude: ". . . and of $\delta X/\delta t$ taken at Borrego, California, U.S.A.". The reference in the text to Fig. 3 should read: "Fig. 3 shows the simultaneous records of $\delta Y/\delta t$ at our base station and of $\delta X/\delta t$ near Borrego Springs . . . ".

CO-ORDINATION CHEMISTRY

THE Fourth International Conference on Co-ordination Chemistry was organized by the Chemical Society and held in London under the sponsorship of the International Union of Pure and Applied Chemistry during April 6–11. Since 141 contributions were received (from twenty-three different countries) in addition to seven invited lectures, it proved necessary to hold three concurrent sessions for the reading of papers. The following report is therefore necessarily based on direct attendance at only a sample of the papers presented and otherwise on the preprinted abstracts.

Prof. K. Ziegler (Mühlheim) in the first of the general lectures began by giving an account of the various steps involved in the catalytic polymerization of olefines by aluminium alkyls and concluded with some remarks on the influence of titanium salts on this reaction. The latter topic was taken up in a paper by G. Natta and G. Mazzanti (Milan), who presented evidence on the structures of some mixed complexes of titanium and aluminium which may be involved. The mechanism of the reaction between aluminium alkyls and titanium halides was further discussed in a paper from Israel.

Dr. H. M. N. H. Irving (Oxford) reviewed the available information on the stability of metal complexes in solution and showed how some simple theoretical ideas could be used to establish useful correlations. Among the many interesting contributions on this topic one may mention a study of thio-complexes from G. Schwarzenbach's laboratory in Zürich, a paper on the heats of formation of ethylenediamine complexes by M. Campolini and co-workers (Palermo), a study of polynuclear copper (II) complexes of carboxylic acids by D. L. Martin and F. J. C. Rossotti (Edinburgh) and work on silver (I)–oxine complexes by D. Dyrssen and collaborators (Stockholm).

Prof. H. Taube (Chicago) reviewed recent work on the mechanisms of complex ion reactions in solution and described some entirely novel experiments of his own. He provided conclusive proof that during the course of the oxidation–reduction reaction between cobalt (III) and chromium (II) ions under appropriate conditions, electrons are transferred through the whole length of the terephthalic acid molecule, and further showed that if the methyl ester of terephthalic acid was present, it was hydrolysed in the course of the reaction. This work opens the way for a full-scale attack on the vexed problem of electron transport through conjugated systems, and should have important consequences.

Studies on the mechanisms of the photochemical reactions of complex ions were reported by S. T. Spees and A. W. Adamson (University of Southern California), who discussed the possible role of doublet states in the photochemistry of chromic complexes; another paper on this subject was given by D. R. Stranks and G. J. Weston (Leeds). Contributions on the detailed kinetics of the hydrolysis of chromic complexes were presented by J. Bjerrum and co-workers (Copenhagen), who infer the existence of the $[\mathrm{Cr\ en_2(enH)\ (H_2O)}]^{4+}$ ion as an intermediate in the hydrolysis of $[\mathrm{Cr(en)_3}]^{3+}$, and by H. L. Schläfer (Frankfurt am Main), who studied the equation of $[\mathrm{Cr\ Ox_2\ en}]^{-}$.

Dr. Greenberg presented the results of some recent studies from the U.S.S.R. on the *trans* effect in the substitution reactions of platinum (II) which suggest that the experimental situation is more complicated than has been previously realized. The first studies of the kinetics of the substitution reactions of *bis*cyclopentadienyl titanium dihalides were reported by A. Jensen and F. Basolo (Northwestern University, Illinois). The exchange reaction of quadridentate complexes, particularly of nickel (II), were discussed by W. W. Fee and B. O. West (Adelaide), and the kinetics of the dissociation of complex cyanides and of ethylene–diamine nickel complexes by G. Emschwiller (Paris) and by A. K. Shamsuddin Ahmed and R. G. Wilkins (Sheffield), respectively.

Some of the liveliest discussions followed papers of a rather theoretical nature dealing with the spectra and magnetic properties of complexes, for example, a paper on the relation between the geometrical structure and the magnetic properties of nickel (II) complexes by G. Maki, and another on the effect of the thiocyanate ion on the spectra of metal ions by C. E. Schäffer (Copenhagen). An interesting account of the magnetic susceptibility of rhenium compounds was given by B. Jezowska-Trzebiatowska (Wroclaw). The variation of the magnetic susceptibility of vanadium (III) complexes with temperature was discussed by B. Figgis, J. Lewis and F. E. Mabbs (University College, London). Two papers, one by S. Minc and W. Libus (Warsaw) and the other by F. A. Cotton and R. H. Holm (Massachusetts Institute of Technology), dealt with the physical properties and relative stabilities of the various types of cobalt (II) complex which exist in solution, and two others, one by C. R. C. Coussmaker and collaborators (Oxford) and the other by A. Turco and G. Giacometti (Padua), considered the properties of the versatile complexes of nickel (II) with substituted phosphines.

The X-ray determination of the structure of a complex formed by azobenzene and arsenic trichloride was reported by E. Ferroni and P. Orioli (Florence); the cuprous–diazoaminobenzene complex was shown by I. D. Brown and J. D. Dunitz (Royal Institution, London) to be dimeric in the crystal and to involve an eight-membered ring containing six nitrogen and two copper atoms. M. R. Truter and her co-workers (Leeds) discussed the structure of β-diketo complexes of trimethyl platinum (IV). Other structures described included those of basic zirconium chromates and β-$\mathrm{Zn(OH)Cl}$. An important paper by I. Linqvist (Uppsala) surveyed the structures of some addition compounds of phosphorus oxychloride and selenium oxychloride.

A further group of contributions dealt with the elucidation of molecular and electronic structure by means of infra-red and Raman spectroscopy. K. Nakamoto, P. J. McCarthy and A. E. Martell (Clark University, Worcester, Mass.) discussed the infra-red spectra of the metal complexes of β-diketones, while D. B. Powell and N. Sheppard (Cambridge) dealt with the metal complexes of amines and ethylenediamine and showed that for the latter both *cis* and *gauche* configurations of the ligand are possible. Infra-red spectra of heteropolytungstates were reported by a group of workers from Moscow. Raman spectra of addition compounds of sulphur trioxide were reported from Amsterdam and of stannic chloride from Karlsruhe.

Among the many papers principally concerned with the preparation of new compounds and the elucidation of their reactions one can pick out only a few. S. Herzog and co-workers (Jena) described the extension of their work on dipyridyl complexes of metals in abnormally low valencies to the preparation of the diamagnetic $[Ti(dipyridyl)_3]^-$ ion; L. Naldini (Milan) described a series of salts of the low-spin (hexa-aryl isocyanide)–manganese (II) complexes; V. Cagliotti and co-workers (Rome) discussed the preparation and reduction of the oxygen adducts of cobalt (II)–histidine complexes.

Carbonyls of iridium (III), *iso*cyanides of rhodium (II) and phosphines of osmium (I) were reported by L. Malatesta and S. Sandroni (Milan), by Miss L. M. Vallarino (Milan) and by L. Vaska (Mellon Institute, Pittsburgh), respectively. Complex fluorides of molybdenum and tungsten and rhenium were discussed by G. B. Hargreaves and R. D. Peacock (Birmingham); R. Hoppe and co-workers (Münster) reported on a variety of zirconium, tin and manganese complex fluorides. Heteropolyacids and related polyanionic compounds were treated extensively by groups from Roumania, the U.S.S.R. and Sweden. The properties of volatile nitrato–iron complexes and copper perchlorates were described by C. C. Addison and N. Logan (Nottingham) and by B. J. Hathaway (Hull), respectively.

The subject most completely covered both in general lectures and contributed papers was that of organo–metallic compounds involving transition metals. Dr. E. O. Fischer (Munich) surveyed experimental work on compounds involving 'sandwich' bonding in a comprehensive and lucid fashion. Prof. R. Nast (Heidelburg) described in detail his important researches on the complex acetylides of the metals; the least stable it appears are spontaneously explosive and the more stable only pyrophoric. Dr. H. W. Sternberg (Pittsburgh) discussed recent experimental work on the reactions of acetylenes, etc., with metal carbonyls and produced some interesting speculations on the relevance of these results to problems both of homogeneous and heterogeneous catalysis. Dr. L. E. Orgel (Cambridge) discussed bonding in zero-valent metal compounds.

Determinations of the crystal structure of some organo–transition metal complexes were reported by A. A. Hock, O. S. Mills and G. Robinson (Manchester); the results were, as usual in this field, very surprising. The infra-red spectrum of chromium dibenzene was described by A. Fritz (Munich). The symmetry of this molecule was discussed at some length. The view of the German school was that theory predicted it to have only three-fold symmetry as argued by E. Ruch (Munich) in a contributed paper. A number of other theoretical chemists (the present author included) held that no definite prediction could be made, but strongly favoured the view that the symmetry would prove to be six-fold. The experimental evidence, it seems, is not yet unambiguous.

A paper by L. S. Meriwether, Marilyn Fiene and G. W. Kennerly established that substitution reactions of a number of nickel carbonyl–phosphine complexes occur by way of a three co-ordinated intermediate rather than by a second-order mechanism. The reactions accompanying the polarographic reduction of iron carbonyls were considered by A. A. Vlček (Prague). There was some discussion of a paper by D. A. Brown (Queen Mary College, London) on the effect of phenyl-substitution on the stability of sandwich compounds.

The preparative work described in the field of acetylene–carbon monoxide chemistry was varied, fascinating, and still largely incomprehensible. G. Natta and co-workers (Milan) discussed the synthesis of succinic acid from carbon monoxide, acetylene and water in the presence of metal carbonyls. They suggested that it required binuclear metal complexes as intermediates and provided good evidence for the occurrence of a peculiar lactone-like derivative of succinic acid as a ligand in certain metal complexes. W. Hübel and E. H. Braye (Brussels) described the numerous new compounds which they have prepared from iron dodecacarbonyl and acetylenes. Some compounds contain aromatic rings, some contain cyclopentadienone, and others cannot at present be formulated in an acceptable fashion (like $C_2H_2Fe_2(CO)_8H_2$, they probably do not have 'acceptable' structures). E. Weiss and W. Hübel described the reactions of cyclopentadienones with metal carbonyls. They demonstrated the ability of cyclopentadienone in certain sandwich compounds to behave more like the anion derived from a phenol than like a normal ketone. Presumably this is due to charge-transfer from the metal to the oxygen of the ring.

The insertion of carbon monoxide into organic molecules by way of metal carbonyls was part of the theme of some of the general lectures. It was discussed in detail for the case of alkyl and acyl manganese carbonyls by T. H. Coffield and co-workers (Ethyl Corporation Laboratories, Detroit), who described some carbon monoxide exchange studies which throw considerable light on the reaction mechanisms involved. L. Kirch and M. Orchin (Cincinnati) described recent experimental work on the oxo-reaction.

Contributions on other metal alkyls included a discussion of the reactivity of the cadmium compounds by J. Vène (Rennes), a paper on alkyl and aryl palladium compounds by G. Calvin, G. E. Coates and P. S. Dixon (Durham), and another on the determination of Grignard reagents by F. G. Mann and I. T. Millar (Cambridge).

A group of papers described catalytic reactions other than those in the carbonyl field. One may mention that of W. Brackman (Royal Dutch Shell, Amsterdam), who described a series of copper–amine complexes which catalyse the oxidation of alcohols, and that of M. T. Beck (Szeged), who described much interesting work on catalysis that has been carried out in Hungary.

Of the papers not directly concerned with metal chemistry I shall mention one, the presidential address of the Chemical Society, which was open to all members of the Congress. Prof. H. J. Emeléus outlined the experimental situation in the field of inorganic polymeric molecules and amply illustrated his thesis that this is a fascinating and largely unexplored region of inorganic chemistry.

The Conference, seen as a whole, left one with no doubt that co-ordination chemistry has entered a period of rapid growth and is already invading fields which traditionally were distinct from it. The development of the various syntheses of large conjugated molecules from carbon monoxide and acetylene can scarcely fail to influence organic chemistry. The close contact between ligand field theory and experiment in the field of co-ordination chemistry provides, perhaps for the first time, a climate in which experiments are designed to test the quantitative predictions of electronic theory; this must prove beneficial to both.

The organization of the Conference, both of the scientific meetings and the more social occasions, was uniformly excellent. All those who were present must be grateful to the members of the Chemical Society committees who were responsible for it and to those industrial concerns which, by their financial support or by acting as hosts, helped to make the meeting so successful.

L. E. ORGEL

THE BRITISH COAL UTILIZATION RESEARCH ASSOCIATION

TWENTY-FIRST ANNIVERSARY OPEN DAYS

THE aim of the Association, from the time of its inception in 1938, has been "to promote research and other scientific work in connexion with the utilization of coal and its derivatives". Some of the achievements of twenty-one years were displayed at the research station during April 22–24.

In 1938, nine experimentalists worked in a single room, 12 ft. square, in Victoria Street, London. To-day the British Coal Utilization Research Association occupies a 20-acre site at Leatherhead, and is one of the largest of the thirty-nine industrial research associations supported by the Department of Scientific and Industrial Research; of its total staff of some 300, eighty are graduates or equivalent and a similar number are research assistants, representative of most of the recognized fields of physical science, from mathematics through the several branches of chemistry and physics to large-scale engineering.

The interests of the Association are many-sided, and this was reflected in the distinctive character of each of the three open days. April 22 was primarily 'members' day'; through its membership the Association forms a link between the four nationalized industries (coal, gas, electricity, transport) and about 150 other members (comprising individual firms and trade associations) which include industrial appliance makers, coal distributors and coal consumers. The Minister of Power, the Right Hon. Lord Mills, was the guest of honour, and in addressing a large and distinguished gathering at luncheon, he observed that the occasion marked the coming-of-age of an Association which had long since established itself as one of the most important and progressive industrial research organizations in Britain.

On the second day the guests were mainly drawn from the field of research; Government departments, research associations, universities and technical colleges were strongly represented. On the morning of the final day parties from local colleges and schools predominated, thus emphasizing the practical interest taken by the British Coal Utilization Research Association in educating young people in the science and technology of coal. In the afternoon the Association was honoured by a visit of a party from the London Section of the Royal Institute of Chemistry; and the day was fittingly concluded by a lecture to this party and other chemists by Prof. R. G. W. Norrish on recent work at Cambridge on flash photolysis in gases.

Throughout its history the British Coal Utilization Research Association has been in close touch with university thought and investigation and has itself maintained a strong programme of basic research. One well-known example of the effectiveness of this approach is the outcome of the experiments on coal breakage which were started in that small overcrowded laboratory in London in 1938. After some years of investigation, in collaboration with the British Colliery Owners Research Association, a specification for grading coal by size was drawn up, and this has been accepted by the National Coal Board as a basis for preparing and marketing coal. Another example of the application of basic research, also exhibited in the Physics Department, was the cone mill. Following a survey of the factors determining the power required for grinding coal to a given size, determination of the Hardgrove grindability index, and measurement of the intrinsic physical and mechanical properties of coal, a matrix theory of coal breakage was developed and the first cone mill was built to test this theory: now its engineering utility is being studied.

Some of the modern techniques being used to investigate both the chemical and the physical aspects of coal constitution were displayed. Research into the chemical basis of the plastic softening of coals, with the view of achieving better control of coking properties, has recently made considerable progress, and current knowledge of the mechanism was illustrated diagrammatically alongside the special apparatus employed. Another exhibit was of interest as the first complete conversion, in a single step, of coal to chemical products without simultaneous production of tar or solid residue: low-rank coals have been treated with chlorine trifluoride, producing a range of chlorofluorocarbons (from colourless oils to resin-like solids) possessing chemical and physical properties that indicate their possible suitability for certain industrial applications.

Considerable work by the Association over a number of years on the ultra-fine porous structure of coal and its development during carbonization has led to the placing, by the U.K. Atomic Energy Authority, of a research contract for fundamental work on the graphite used as moderator in nuclear reactors. This investigation has already shown that closed pores in the graphite become accessible during its reaction with oxidizing gases, and an estimate of the importance of internal burning has been obtained.

Among the current major problems facing the coal industry are: improvement of methods for using small coal; meeting the challenge of competition from oil; and assistance in the implementation of the Clean Air Act. Research by the Association has, therefore, been directed especially towards: (*a*) improving and devising appliances suitable for burning small coal; (*b*) developing methods for the automatic control of combustion; and (*c*) investigations on reduction of atmospheric pollution from coal-burning appliances.

One of the most important current needs is a method of converting small coal cheaply to gas, and ultimately to oil. The Association's experimental slagging gasifier, built under contract with the Ministry of Power, at present consumes about a ton of fuel an hour and can take, in short tests, up to half of this in the form of pulverized coal. It has been operated successfully at various ash-levels and over a range of ash fluidities. Background studies have made possible the tentative correlation of slag viscosity–temperature curves with slag composition ; and improved methods of analysis have enabled the important constituents of ash to be determined at the rate of four samples a day.

The automatically controlled small-pipe, forced-circulation central heating system, developed by the Association, is being actively promoted by the Coal Utilization Council, and was displayed by them in the exhibition they had arranged on the site. Also on view in the Council's exhibition were some of the thirty or more designs of free-standing convector fire with restricted throat, a type of appliance that has been developed by the British Coal Utilization Research Association.

The Association's Calorimeter Room has taken its place as an absolute standard for testing domestic appliances. A method of automatic control for miniature chain-grate stokers, used to fire central-heating boilers (½–2 million B.T.U./hr.) in offices or blocks of flats, has been devised, and a unit burning ½-in. small coal smokelessly and at high efficiency is now being tested.

An air–fuel ratio controller has been developed within the Association for fitting to stokers of Economic and Lancashire boilers in order to take much of the responsibility for maintaining the correct ratio of fuel to air out of the hands of the fireman, and one of these controllers was in use on the boiler used for site heating.

A first step towards finding means for reducing atmospheric pollution from coal-burning appliances has been made through the work on the measurement of dust and grit emission from boiler furnaces. The methods of sampling dust from stacks developed by the Association were on view and have aroused much interest in those concerned with enforcing or complying with the Clean Air Act. The automatic particle-sizing apparatus developed by the Association was displayed ; with special care it can be employed down to 2 microns and can be used to carry out eight analyses a day.

The study of problems arising from the deposition of inorganic solids and corrosive liquids from flue gases in water-tube boilers forms an important part of the Association's work ; these problems are investigated both in the laboratory and at power stations. Large- and small-scale equipment used in these investigations was on view. Special measuring apparatus devised for this work was also demonstrated.

It has not been possible in this short account to mention more than a selection of the exhibits. A fuller account of the current researches is contained in the annual report of the British Coal Utilization Research Association for 1958, and a bibliography of the Association's publications during 1938–59 is to be published in the near future.

THE EAR UNDER WATER

A DISCUSSION meeting devoted to "The Ear under Water" was held at the Royal Society on March 12. In his opening survey, Prof. O. Lowenstein pointed to the fact that even in its most highly evolved state the vertebrate ear is a dual—or even triple—purpose sense organ. It incorporates receptors for angular acceleration (semicircular canals), for linear acceleration including gravitational stimuli (otolith organs) and for oscillatory changes in linear acceleration such as vibration in general and sound in particular (otolith organs, cochlea). The vertebrate ear appears to be a phylogenetic novelty derived by modification from the lateral-line organs of early fish-like vertebrates and not from the statocyst of the invertebrates. Thus, the ear is probably not the comparative-anatomical homologue of the invertebrate statocyst. There is no doubt, however, that the two organs are functionally analogous. It was therefore considered desirable to review recent work on the invertebrate statocyst in the context of the symposium.

Dr. Melvin Cohen (University of Oregon) described the anatomy of the statocyst of the lobster, *Homarus americanus*, and discussed the results of an electrophysiological analysis of its function. It contains two types of position receptors, one for the monitoring of absolute position and one which also indicates the direction from which a certain position is approached. A third receptor type functions as an acceleration receptor and is insensitive to position. There are receptors responding to vibration of the solid substrate, but no reactions to air- or water-borne sound could be registered. Dr. Cohen pointed to the striking similarities between the responses from the crustacean statocyst and those from the various end organs of the vertebrate labyrinth.

In a paper on the cephalopod statocyst, Prof. J. Z. Young gave a detailed description of the morphology of the statocyst of the octopus. This remarkable sense organ, too, shows a most interesting and functionally suggestive number of items of structural convergence with the vertebrate labyrinth. Apart from a vertically placed macula with otolith, there is a crista which has sections in three planes of space, each section being associated with a separate nerve. The sensory hairs are ensheathed in a matrix of unknown composition forming cupulæ reminiscent of those found in the labyrinth. Large neurons having dentritic endings as well as hair processes underlie the sensory cells of the crista and appear to make synaptic contact with them, although the hair cells themselves are primary sensory cells equipped with centripetal axons. A hand-shaped vane (the so-called anti-crista) protrudes into the endolymphatic space and seems to be so arranged as to protect the vertical section of the crista from overstimulation when the octopus suddenly accelerates forward, as it does on attacking prey.

Prof. Young stressed that there is no behavioural evidence of hearing in the cephalopods, but on anatomical grounds there is no reason why the cephalopod statocyst should not be potentially capable of vibration reception or even hearing, besides its manifestly obvious function as an organ of static and dynamic spatial orientation.

The vertebrate ear evolved in aquatic animals, and it may well be that its function as a vibration receptor evolved simultaneously with that of an organ of orientation. As an introduction to the problems connected with hearing in aquatic vertebrates, Dr. P. Vigoureux (National Physical Laboratory, Teddington) gave a most useful survey of the physical aspects of sound propagation under water. So far as penetration of sound from air into water is concerned, there is a critical angle of 13° of reflexion at the interface between air and water, and total reflexion occurs at all greater angles of incidence. Sound can therefore penetrate into water only if its incidence is almost vertical. Yet the human ear is sensitive enough to hear under-water sound from a powerful source in the air overhead. Dr. Vigoureux also discussed some effects of temperature gradients leading to conditions of exceptionally good sound propagation over long distances. Sound absorption is only 1/1000th part of what it is in air, and this is yet another reason for the considerably greater distance of sound propagation in water.

Prof. S. Dijkgraaf (Utrecht) introduced his account of hearing in bony fishes by a definition of sound and hearing. This has for a long time been a controversial matter and he advocated ascription of the ability of hearing to such animals as are sensitive to a succession of pressure waves propagated with a characteristic velocity through the medium, be it air or water, and able to detect these stimuli by means of special receptors exclusively used for this purpose. If the latter condition is not fulfilled, one should speak of sound- or vibration-reception instead of hearing.

Prof. Dijkgraaf distinguished among the bony fishes between what he called 'specialists' and the normal run of fishes. The 'specialists', mostly fresh-water fishes, have been shown to possess sound-reinforcing structures like the Weberian ossicles or special gas chambers connected with the ear. Their frequency-range is considerable and they are more highly sensitive to tones than man up to a frequency of 1,000 c./s. They are also capable of pitch discrimination over a limited range (up to 1,260 c./s.) and can discriminate frequency differences as low as 4 per cent. However, no evidence for directional hearing has so far been obtained. So-called normal fishes (almost all marine forms) have an upper limit of 400–1,000 c./s. and a much higher threshold.

In the second part of his paper, Prof. Dijkgraaf dealt with the problem of functional localization of hearing within the labyrinth of bony fishes and discussed the part played by the otolith organs in the sacculus and lagena in some, and the probable role of the utriculus in other forms, depending on differences in the nature and topographic deployment of the sound-reinforcing structures. Tactile skin receptors may be involved in the reception of low-frequency sound, but there is no evidence for the collaboration of the lateral line.

In higher vertebrates the ear became adapted to the reception of airborne sound. The special matching devices of the middle ear and the range-finding pinna of the mammals were evolved. Papers by Dr. Reysenbach de Haan (Eindhoven) on aspects of mammalian hearing under water and by Dr. F. C. Fraser and Mr. P. E. Purves of the British Museum on the osteology, acoustic matching, and evolution of air sinuses, and on muscular and vascular arrangements, acoustic isolation, and directionality of hearing, dealt with the way in which the Cetacea solved the problems of underwater hearing on their return to a fully aquatic existence.

Dr. Reysenbach de Haan pointed out that under water the external ear and the middle ear of the terrestrial mammal become useless. Man has no directional hearing under water and suffers a loss in hearing of 60 db. Whales and dolphins rely chiefly on sound for their orientation, and yet they have no outer ears and their auditory meatus has become highly modified. Dr. Reysenbach de Haan believes that the modified structures corresponding to the meatus are devoid of function, as the rate of transmission of sound in the tissues around the external auditory canal is practically equal to that in water. The bulla, however, is filled with air and kept hermetically sealed from the water outside. The striking feature of the middle ear or bulla is that it has parted company with the skull and, like the inner ear in the petromastoid, has come to hang loose under the skull. Foam-filled sinuses in the petromastoid are in communication with the air of the middle ear in the bulla and via the Eustachian tube with the air of the respiratory passages. The inner ear is thus completely air-insulated from the surrounding tissues, from the skull, and from the surrounding water. The two ears are also completely insulated from one another. This, Dr. Reysenbach de Haan held, was an indispensable condition for successful directional hearing under water.

Modifications of the middle ear and also of the cochlear structures were demonstrated to be associated with the sensitivity of the Cetacea to supersonic frequencies higher than 100,000 c./s. Cetaceans produce high-pitched sound and are known to echolocate like bats. In water, with the four times longer wave-length, much higher frequencies are necessary for the detection of objects of the same size.

Experiments on the directional hearing of dolphins and the methods used in the capture of these animals in Danish waters and their transport to the Netherlands were illustrated by a film made by W. H. Dudok Van Heel (Holland).

In their communication on the anatomy and function of the cetacean ear, Dr. F. C. Fraser and Mr. P. E. Purves, of the British Museum of Natural History, dealt with the morphology of the auditory meatus in toothed whales and whalebone whales. They have come to the conclusion, contrary to the opinion voiced by Dr. Reysenbach de Haan, that the meatus is not devoid of function. They believe that it plays an important part in sound conduction.

Experiments on a large portion of the squamomastoid region of a fin whale, preserved by deep-freezing and dissected after thawing to expose the middle ear, the wax plug and meatus, showed that the attenuation of high-frequency sound waves (100,000 c./s.) was considerably lower when conduction followed the meatus with its lengthwise orientated fibre system, than in the surrounding tissues in which the fibrous structures are randomly orientated. The authors assumed that sound transmitted by the meatal path would be dominant at any level of intensity. The animal must be subjected to an intensity and/or phase difference at the cochleæ of the two ears due to the screening effect of the head and the distance separating the two meatal openings. This may be of vital importance for directional hearing.

A detailed description of the air sinuses and peculiarities of the vascular system served to emphasize the acoustic isolation of ear from skull and jaws and ear from ear. The part played by the albuminous foam formed by nitrogen in an oil–mucus emulsion was discussed, and it was shown how this foam can remain persistent even during a prolonged dive.

Finally the modifications of the middle ear ossicles were described with reference to the requirement for successful matching of the cetacean ear to water-borne sound. They were illustrated by a working model.

A series of anatomical exhibits was shown to illustrate the specialization in the topographic relationship between ear and skull, especially the arrangement of air sinuses in the various cetaceans.

The contributions to the symposium will be published in full in the *Proceedings of the Royal Society*.

O. LOWENSTEIN

THE INDIAN ASSOCIATION FOR THE CULTIVATION OF SCIENCE

THE annual report for 1957–58 of the Indian Association for the Cultivation of Science*, which includes lists of papers published during the year under their departmental headings, records further work on the thermal diffusion and inter-diffusion of gases. An apparatus has been designed for measuring the thermal conductivity of diffusing gases and a new apparatus constructed for purifying high-pressure commercial hydrogen. The dimensions of the unit cell of naphthazarin have been re-determined by X-ray methods and further work on the molecular structure of this crystal is in progress. The work of the Department of Magnetism was reorganized and the study of paramagnetic anisotropy of dihalides of copper(II), the paramagnetic behaviour of fluosilicates and chlorostannates of copper(II) and measurement of the principal susceptibilities of paramagnetic crystals down to liquid-hydrogen temperatures has been undertaken, as well as the study of paramagnetic crystals both by the paramagnetic electron resonance and the proton resonance method. The anisotropy of many nickel(II) salts of similar constitution was studied to ascertain the effect of long-range crystalline fields in these salts, and work on paramagnetic alums of titanium(III), vanadium(III) and chromium(III) was completed.

In the Optics Department the Raman spectra of *o*-chlorophenol in different solvents, of α- and γ-picoline and their solutions in alcohol in liquid and solid state, and of ethylbenzene, chlorobenzene and bromobenzene in the frozen state at − 180° C. have been determined and the ultra-violet absorption spectra of many aromatic compounds studied in the vapour, liquid and solid states, as well as those of frozen 0·2 per cent and 25 per cent solutions of the dichlorobenzenes in *iso*-butyl alcohol at − 180° C. and the Debye–Scherrer patterns due to frozen toluene, chlorobenzene and bromobenzene and to diphenyl at 32° C. and at − 180° C. The Department of Theoretical Physics was concerned mainly with the spin of an electron from five-dimensional wave equations, the influence of constant electric and magnetic fields on the spin of the particle, electronic energy bonds in lattices and some generalizations in relativistic cosmology.

In the Department of Physical Chemistry, investigations in high polymer chemistry related to the kinetics and chain transfer behaviour of methyl *iso*propenyl ketone, the aqueous polymerization of vinyl monomers in redox systems, the thermodynamic properties of binary mixtures, the determination of absolute values of the rate constants in polymerization and the preparation and properties of soil conditions of the krillium type. In general and analytical chemistry, work is being carried out on the mutual solubilization of oils and water, the decomposition of peroxides in different solvents and the velocity of ultrasonic waves in solutions and liquids. An apparatus has been assembled for determining the mutual solubilities of organic compounds *in situ*. The Department of Organic Chemistry continued its investigations on sesquiterpenoids, diterpenoids, triterpenoids and steroids, and in the Department of Inorganic Chemistry attention was concentrated on the study of co-ordination complexes and their applications in analytical chemistry. It has been shown that 3- and 5-oximinomethylsalicylic acids and 3- and 5-aldehydosalicylic acids can be used for estimating thorium and its separation from the cerite earths.

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* Indian Association for the Cultivation of Science. Annual Report for 1957–58. Pp. 52. (Jadavpur, Calcutta: Indian Association for the Cultivation of Science, 1959.)

THE EAST AFRICAN INDUSTRIAL RESEARCH ORGANIZATION

REPORT FOR 1957–58

THE annual report for 1957–58 of the East African Industrial Research Organization* records the official opening of the new headquarters of the Organization in Nairobi on February 14, 1958, and spectacular results from a close collaborative study by the Fuel Advisory Service with the Research and Economy Section of the Chief Mechanical Engineer's Department of the East African Railways and Harbours, notably in the design of a special burner for lighting up locomotive boilers and in increasing the power developed by locomotive engines in service, using a Giesil ejector. Advice was also given on the utilization of wood waste, and fuel economies of 5–20 per cent were demonstrated in some thirty factories. An oil-fired incinerator was designed for the new swine fever research centre at Mugaga and a similar but larger one for the new Wellcome Foot-and-Mouth Disease Centre.

The Department of Fuel Technology and Chemical Engineering has also examined the use of solar driers and the dust-proofing of motor cars. Extensive work on the mechanical drying of Arabicz coffee has shown that damage is reduced by pre-drying and increased by increasing the final drying temperatures, and that daylight has a marked effect on the liquoring quality of the dried bean. The range of light frequencies responsible is now being studied, and apparatus has been constructed for the determination of moisture content and desorption isotherms using a wet- and dry-bulb technique with recirculated air flow. Two full-scale driers for use on wet groundnuts were designed and tested for the National Institute of Agricultural Engineering and the Tanganyika Agricultural Corporation.

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* East Africa High Commission. East African Industrial Research Organization Annual Report, 1957–1958. Pp. ii+18. (Nairobi: Government Printer, 1958.) Sh. 2.

Work on the production of vitreous bowls should now permit costs of production to be estimated. Successful large-scale trials of locally made refractory bricks and bonding cement for setting them in locomotive fire-boxes are reported. Much work was done on the elimination of arsenic from cement copper prepared from an ore containing arsenic and on the production of high-grade silicophosphatic fertilizer by the low-soda process.

PART-TIME WORK FOR WOMEN GRADUATES

IN 1956, as an experiment, an agency was started in the London area to put women graduates in touch with any suitable part-time work. From the beginning it was hoped that the agency might not only help to canalize existing opportunities but also increase them. Many potential employers are prejudiced against part-time workers; it was felt that they might have more confidence if they could interview not one but a number of suitable candidates for each vacancy, and feel that they could call on a reserve if the need arose.

Some types of work, such as highly responsible administrative posts, could not be adapted to part-time hours, but other types could: teaching, research assistance, information work, indexing, cataloguing, translation, abstracting, statistical work all seemed possible to arrange in this way. It also seemed clear that much of this work could be done at home and that it would be greatly welcomed, especially by mothers of young children. The growth of the agency has recently been described by Mrs. D. D. Furley (*Univ. Rev.*, 31, No. 2; February 1959).

The agency started in a modest way with a nucleus of about twenty graduates in London who were in search of part-time work. At first, few vacancies were notified to the agency. After the appearance of one or two letters to the Press from people who had heard of the scheme, about three hundred graduates registered as potential part-time workers in the London area and letters were received from about five hundred others living outside the London area who were seeking work, but did not realize that the scheme applied only to London.

Many employers were sympathetic to the idea and more jobs gradually became available.

In the first eighteen months, 378 jobs were notified to the agency, and 260 of them were filled by graduates registered with it. In the following twelve months, 440 jobs were notified, and 303 were filled. The majority of these jobs were in teaching, research of one kind or another and editorial or secretarial work. The figures included both temporary and permanent jobs; several women who started by filling some temporary vacancy have later been found permanent part-time jobs by the same employer.

It is impossible to fill some of the vacancies notified to the agency. There are many reasons: part-time science teachers are as rare as full-time ones; there is more demand than supply for good secretaries; the pay offered is sometimes, and particularly in social work, unattractive; and vacancies are often separated from the likeliest candidates by a journey of impossible complexity and length.

Fewer permanent than temporary jobs are filled. This seems to reflect a general reluctance on the part of married women to commit themselves to permanent work. Women who have not held a job since marriage or since having children are sometimes uncertain how it will work out. Mothers are always reluctant to commit themselves to working during school holidays and permanent jobs which conform to school holidays are very hard to find.

In May 1957 a similar agency was opened in Manchester. Although similar to the London agency, in one way it differs from it. As Manchester is a smaller and non-metropolitan city, it was thought advisable not to confine the agency to graduates, but to use it for other women with comparable qualifications—diplomas, teachers' training certificates, or knowledge of foreign languages. Eighteen months experience in Manchester bear out the findings of the London agency.

Altogether, more than a thousand women, about 800 of them married, have registered with the London agency since its inception. Although about 40 per cent of them have been 'housebound' by children, illness or elderly relatives, approximately half of them have found work through the agency. In Manchester more than one hundred women have registered, all but nine of whom are married; sixty of these have a university degree, twenty-three a diploma of one kind or another. Forty-six of these have found temporary or permanent work through the agency.

MIGRATION AND DISPERSAL OF NEW ZEALAND GANNETS

A TOTAL of 3,999 gannet chicks was banded at Plateau station, Cape Kidnappers, Hawke's Bay, and Horuhoru station, Hauraki Gulf, New Zealand, between 1951 and 1957. Up to March 31, 1957, 207 recoveries were made. These recoveries include 26 chicks which had not left the gannetry, 146 birds recovered outside the gannetry, and 35 live sub-adult birds caught on their return to Plateau gannetry. An account of the investigation has been given by Kazimierz Wodzicki and Peter Stein (*Emu*, 58, Part 4; September 1958).

The percentage of recovery for the whole period was 3·1 (3·3 from Plateau and 2·9 from Horuhoru). This distribution of recoveries throughout the year shows two periods of increased mortality; one affecting first-year birds within the first few months of their independent life and associated with the crossing of the Tasman Sea; another peak occurring in late spring and summer and comprising one- to two-year-old birds.

It was found that fully fledged chicks leave the gannetry at the age of 15½ weeks. The majority of Plateau gannets take a northern route towards the North Cape; others migrate along the eastern coast of North Island and reach Australia through Cook Strait. Recoveries of Horuhoru gannets show an almost exclusive use of the northern route. At the age of 24 weeks all but sickly or late chicks cross the Tasman Sea with an average speed of up to 240 miles a day.

In Australia young gannets disperse widely from subtropical waters in the south and to the Indian Ocean pelagic waters in the west. Horuhoru birds tend to go further south than those banded at Plateau. There seems to be no appreciable difference in geographical distribution among various age-groups of the sample. Sub-adult gannets remain in Australian waters until they are two to three years old.

From that time an increasing number of recoveries is made in New Zealand, where the birds disperse around the coast, and there appears to be some difference in the geographical distribution of recoveries from the two stations.

An analysis of live birds recovered at the gannetry shows that young gannets begin to reappear at their home-gannetry at the age of three years, first as 'roosting' or 'unemployed' birds; from the age of 4–5 years they commence to breed, but at the age of 6–7 years only about half of the birds are breeding.

In all three subspecies of the gannet there is a similar strong urge in juvenile birds to migrate to warmer seas; a similar maximum distance of about 4,000 miles may be flown by the three subspecies, but whereas North Atlantic and Cape gannets move towards the equator, New Zealand-bred Australasian gannets migrate westwards.

BIOSYNTHESIS OF CELL CONSTITUENTS FROM C_2-COMPOUNDS

Formation of Malate from Glycollate by *Pseudomonas ovalis* Chester

DURING the growth of micro-organisms, intermediates of the tricarboxylic acid cycle are utilized to provide the carbon skeletons of many cell constituents[1,2]. When C_2-compounds are the sole source of carbon, means must exist whereby such intermediates, drained from the cycle, are replenished by ancillary reactions. When the C_2-substrate for growth is acetate, this is accomplished via the glyoxylate cycle[3–5], in which the decarboxylative steps of the tricarboxylic acid cycle are replaced by the overall reaction:

$$\text{acetate} + iso\text{citrate} \rightarrow \text{succinate} + \text{malate} \qquad (1)$$

Reaction (1) is the sum of two reactions, catalysed respectively by *iso*citratase[6,7] and by malate synthetase[8]. Experiments on the influence of growth substrates on the formation of *iso*citratase[9] have shown, however, that this enzyme is formed only when acetate or a precursor of acetate (such as octanoate[10]) serves as growth substrate, and that cells grown on C_2-compounds other than acetate (such as glycollate, glycine or oxalate) contain only negligibly low amounts of *iso*citratase. Other routes must therefore exist for the necessary syntheses of tricarboxylic acid cycle intermediates from these C_2-compounds.

The purpose of this communication is to show that cells grown on glycollate contain enzymes capable of forming malate from glycollate, and to suggest a possible route (Fig. 1) for the formation of cell constituents from glycollate. The evidence for this suggestion rests on the following observations:

(1) Washed suspensions of *Pseudomonas ovalis* Chester grown on glycollate readily oxidized glycollate, glyoxylate, pyruvate and all intermediates of the tricarboxylic acid cycle, indicating the occurrence of that cycle under these conditions.

(2) Extracts of such cells, obtained by supersonic disintegration and centrifugation, readily catalysed the formation of glyoxylate from glycollate. Fractionation of such extracts with ammonium sulphate indicated that this enzyme, which catalysed the reaction:

$$\text{glycollate} + A \rightarrow \text{glyoxylate} + A.2\text{H} \qquad (2)$$

where A is an unknown electron acceptor, was largely concentrated in that fraction precipitable between 0 and 35 per cent saturation with ammonium sulphate. The bright yellow colour of this fraction, and the finding that its ability to oxidize glycollate was enhanced by the addition of phenazine methosulphate (0·1 per cent w/v), suggest that reaction (2) may be catalysed by a glycollic oxidase, possibly similar to that described in spinach leaves[11], in which case the electron acceptor A would be a flavoprotein.

(3) When glyoxylate was incubated anaerobically with crude sonic extracts of cells grown in glycollate, carbon dioxide was rapidly evolved. In order to establish the stoichiometry of this reaction, the crude extracts were fractionated with ammonium sulphate (35–50 per cent saturation), dialysed, and eluted from columns of diethylaminoethyl cellulose with portions of phosphate buffer, pH 7·5, of increasing strength. When the fraction eluted by 0·1 M buffer was incubated with 6·7 μmoles of glyoxylate, 3·4 μmoles of carbon dioxide were evolved; this is quantitatively in agreement with the following reaction:

$$2\ \text{glyoxylate} \rightarrow CO_2 + C_3\text{-compound} \qquad (3)$$

observed by Krakow and Barkulis[12] with extracts of *E. coli* grown in glycollate. As described by these authors, maximal enzymic activity depended on the presence of magnesium ions and thiamine pyrophosphate.

(4) This purified cell fraction also catalysed the oxidation of reduced diphosphopyridine nucleotide in a reaction dependent on the presence of glyoxylate and enhanced by the addition of magnesium ions and thiamine pyrophosphate. The rate of oxidation of reduced diphosphopyridine nucleotide increased with time, and was more rapid after pre-incubation of the cell fraction with glyoxylate, magnesium ions and thiamine pyrophosphate than when it was present from the start. This suggested that the

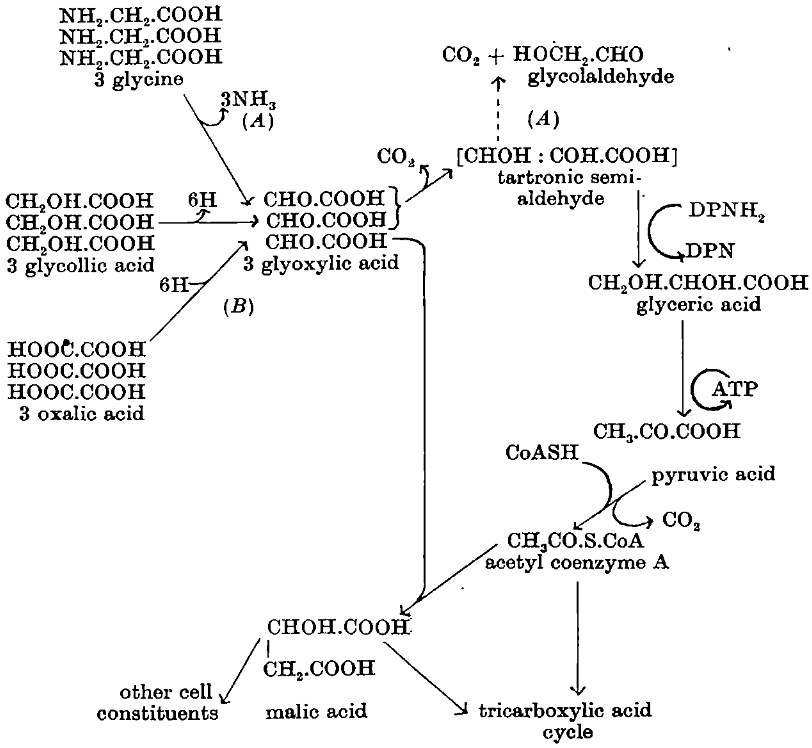

Fig. 1. Possible route for the formation of cell constituents from C_2-compounds by *Pseudomonas*
($DPNH_2$ = reduced diphosphopyridine nucleotide; ATP = adenosine triphosphate; CoASH = coenzyme A)
(*A*) see Callely and Dagley (second communication); (*B*) see Quayle and Keech (third communication)

compound reduced by reduced diphosphopyridine nucleotide was not glyoxylate, but a material derived from glyoxylate.

(5) In the presence of thiamine pyrophosphate and excess reduced diphosphopyridine nucleotide, the purified cell fraction catalysed the formation of 1·8 μmoles of glyceric acid for the utilization of 3·5 μmoles of glyoxylate. No glyceric acid was formed when reduced diphosphopyridine nucleotide or glyoxylate was omitted, or when the cell fraction was boiled prior to incubation.

(6) In the absence of reduced diphosphopyridine nucleotide, the purified cell fraction catalysed the conversion of [1-^{14}C] glyoxylate to carbon-14 dioxide and an unknown material, which was capable of reacting with acid 2,4-dinitrophenylhydrazine to form a radioactive derivative. On addition of alkali, this derivative lost most of its radioactivity and gave a spectrum indistinguishable from that of the *bis*-2 : 4-dinitrophenylhydrazone of glyoxal (max. light absorption at 570 mμ). In the presence of reduced diphosphopyridine nucleotide, this unknown material did not accumulate; instead, 1 molecule of radioactive glycerate was formed for each molecule of carbon-14 dioxide evolved and for each 2 molecules of [1-^{14}C] glyoxylate utilized. No labelled glycollate was found, which showed that glyoxylic reductases[13,14] were absent from this cell fraction.

(7) The incorporation of label from [1-^{14}C] glyoxylate into glycerate by the purified cell fraction was not affected by addition of hydroxypyruvate, and the hydroxypyruvate re-isolated after the incubation was devoid of radioactivity. The purified cell extract did not catalyse the oxidation of reduced diphosphopyridine nucleotide in the presence of hydroxypyruvate.

These results indicate that the overall process occurring was the formation of a C_3-compound from glyoxylate by reaction (3), followed by its reduction to glycerate:

$$C_3\text{-compound} + DPNH_2 \rightarrow \text{glycerate} + DPN \quad (4)$$

They further show that, unlike the system described by Krakow and Barkulis[12], the C_3-compound formed by *Pseudomonas* extracts was neither hydroxypyruvate nor any material in ready equilibrium with it. It is conceivable that the unknown C_3-compound is tartronic semialdehyde[15], the ene-diol form of which[16] (HCOH : COH.COOH) might exhibit the properties noted under sections (4)–(7) above.

(8) Crude sonic extracts of cells grown in glycollate formed carbon-14 dioxide and radioactive glycerate from [1-^{14}C] glycollate, this being the sum of reactions (2)–(4).

(9) Crude extracts of cells grown in glycollate prepared in a Hughes press[17] catalysed the formation of pyruvate from glycerate when incubated with adenosine triphosphate, but not when adenosine triphosphate or glycerate was omitted or when the cell extract was boiled prior to incubation.

(10) Crude sonic extracts of cells grown in glycollate readily oxidized pyruvate, presumably via acetyl coenzyme A. Such extracts also contained high activities of malate synthetase[8] and were capable of forming[18] about 7 μmoles of malate/hr./mgm. of protein from acetyl coenzyme A and glyoxylate, as measured by optical assay[19].

Reactions (2)–(4), in conjunction with the reactions leading from glycerate via pyruvate to acetyl coenzyme A, would represent the conversion of two molecules of glycollate to one of acetyl coenzyme A and two of carbon dioxide. Condensation of the acetyl coenzyme A thus formed with one molecule of glyoxylate (derived from the oxidation of a third molecule of glycollate) would yield one molecule of malate:

$$3\ \text{glycollate} \rightarrow \text{malate} + 2\ CO_2 + 6\ H \quad (5)$$

which would serve as the required precursor of cell constituents. The findings described by Callely and Dagley and by Quayle and Keech in the communications following indicate that this or closely similar biosynthetic routes may operate also in pseudomonads grown on glycine or oxalate as sole carbon sources.

Full experimental details of this work will be published elsewhere.

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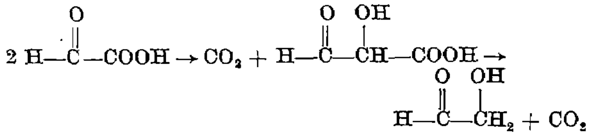
Metabolism of Glycine by a Pseudomonad

Bachrach[1] isolated from the deep litter of a poultry house four species of *Pseudomonas* that utilized uric acid as sole source of carbon and nitrogen for growth. Prof. B. C. J. G. Knight kindly made these strains available, and we have studied the metabolism of glyoxylic acid by '*Pseudomonas A*' grown with glycine as sole source of carbon in aerated mineral salts media at 30° C. Whole cells oxidized various acids of the tricarboxylic acid cycle; and although citrate was attacked only slowly, this may be attributed to slow penetration of the cells by the compound, which was oxidized by cell-free extracts. Glyoxylic acid was oxidized rapidly by cells grown with glycine, but not with succinate as source of carbon. The work of Janke and Tayenthal[2] and Campbell[3] has established glyoxylate as an intermediate in glycine metabolism by species of *Pseudomonas*.

Extracts of cells grown with glycine catalysed the decarboxylation of glyoxylic acid. After disintegration in a Hughes press[4] cooled to −14° C., each 10 gm. of crushed cells was homogenized with 1 gm. of powdered alumina and 25 ml. of phosphate buffer, *p*H 7·2; cell debris and alumina were then removed by centrifuging to give a clear yellowish extract. Manometer flasks filled with nitrogen and fitted with two side-arms contained different amounts of glyoxylic acid (3–17 μmoles) to which 0·5 ml. of extract was added at 30° C. The carbon dioxide released after tipping 0·5 ml. of 3 *N* sulphuric acid from the second side-arm was about 85 per cent of that calculated on the assumption that one mole of glyoxylate gave rise to one mole of gas. Extracts did not oxidize glyoxylate: the same amounts of carbon dioxide were evolved in air as in nitrogen; and no glyoxylate or other keto-acid remained when all gas had been released. The reaction was also conveniently studied by following the rate of disappearance of glyoxylate, determined by the method of Friedemann and Haugen[5]; thus, from 10 ml. of reaction mixture in a boiling-tube at 30° C., 15–20 μmoles of glyoxylate were lost in 10 min. in the presence of 1 ml. of fresh extract. After reaction, the solution contained a compound which formed a derivative with 2 : 4-dinitrophenylhydrazine giving a purple colour with 5 *N* sodium hydroxide; the absorption spectrum showed a maximum at 565 mμ and appeared identical with that of the *bis*-2 : 4-dinitrophenylhydrazone of glycolaldehyde (and glyoxal). The product of glyoxylate decarboxylation reacted with naphtharesorcinol in 23 *N* sulphuric acid to give a green colour; the absorption spectrum was similar to that recorded by Dickens and Williamson[6] for hydroxypyruvate and glycolaldehyde; and calculations based on the extinction coefficient at 660 mμ showed that one mole of glycolaldehyde would be formed from two moles of glyoxylic acid.

By analogy with the reactions[7] for the conversion of pyruvate to acetoin, with β-acetolactic acid as intermediate, the decomposition of glyoxylate may be formulated as follows:



$$2\,H{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}COOH \rightarrow CO_2 + H{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle OH}{|}}{C}H{-}COOH \rightarrow H{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\overset{\overset{\displaystyle OH}{|}}{C}H_2 + CO_2$$

We have not yet succeeded in separating these two enzymes, and our evidence, which is discussed below, for an intermediate step in the formation of glycolaldehyde is therefore indirect.

When extracts (5 ml.) were dialysed against phosphate buffer (4 lit.) for 24 hr. with stirring decarboxylation of glyoxylic acid was catalysed only when thiamine pyrophosphate and magnesium ions (each 1·5 μmole per ml.) were added with extract. Crude extracts catalysed the rapid oxidation of reduced diphosphopyridine nucleotide in the presence of glyoxylate, but this occurred only very slowly after dialysis. When thiamine pyrophosphate and magnesium were added, rapid oxidation of reduced diphosphopyridine nucleotide was restored, as shown in Fig. 1; however, this oxidation was not catalysed when glycolaldehyde was substituted for glyoxylate. Accordingly, it appears that the immediate product of glyoxylate decarboxylation, which we suggest is tartronic semialdehyde, is the acceptor of hydrogen from reduced diphosphopyridine nucleotide; the reduction product would be glyceric acid, although firm identification is hindered by the competing reaction which produces glycolaldehyde. Oxidation of reduced diphosphopyridine nucleotide in the presence of extract was much more rapid with presumed tartronic semialdehyde present than with hydroxypyruvate, which has also been suggested as a product of glyoxylate decarboxylation by *E. coli*[8].

Since it serves as a substrate for transketolase[9], the production of glycolaldehyde by the reactions described may be of significance in relation to carbohydrate synthesis by this organism; but since glycolaldehyde is itself a C_2-compound, *net* synthesis of cell constituents must be accomplished by a reaction sequence such as that proposed by Kornberg and Gotto (first communication), in which pyruvate malate and other tricarboxylic acid cycle compounds are formed. Support for a reaction sequence involving pyruvic acid was given by experiments with whole cells. When harvested from a glycine medium after

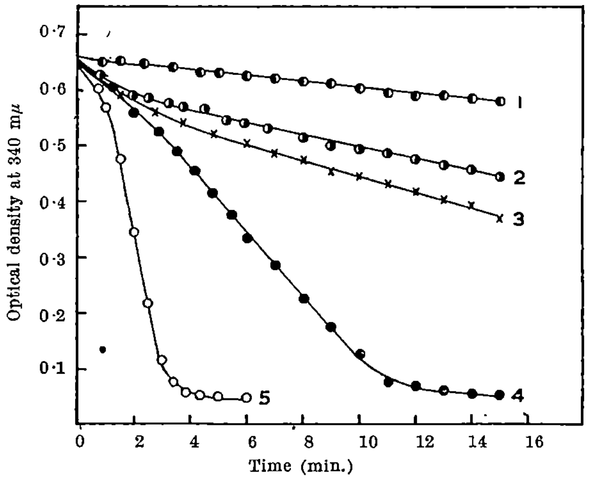


Fig. 1. Oxidation of reduced diphosphopyridine nucleotide by dialysed extracts of '*Pseudomonas A*' grown with glycine. The reaction was started by addition of 0·1 ml. of extract and followed by the fall in optical density at 340 mμ in mixtures made up to a total volume of 3·3 ml. with phosphate buffer (0·015 *M*, *p*H 7·2). Where stated, the following were added: reduced diphosphopyridine nucleotide, about 0·36 μmole; glyoxylic acid, 10 μmoles; thiamine pyrophosphate, 4 μmoles; magnesium sulphate, 5 μmoles. (1) Thiamine pyrophosphate and magnesium ions; no glyoxylate; (2) glyoxylate only; (3) glyoxylate and magnesium ions; (4) glyoxylate and thiamine pyrophosphate; (5) complete reaction mixture of glyoxylate, thiamine pyrophosphate and magnesium ions

about 18 hr. in the stationary phase, a lag in growth of 4 hr. occurred when suspensions were aerated in fresh glycine + mineral salts medium. During this time a keto-acid accumulated of which the spectrum of the 2 : 4-dinitrophenylhydrazone in alkali was identical with that of pyruvic acid; and when cell division began, pyruvate disappeared from the medium. An alternative reaction sequence for pyruvate production from glycine would be by conversion to serine and deamination of the latter; however, extracts from cells grown with glycine contained no serine dehydrase.

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Formation of Glycerate from Oxalate by *Pseudomonas oxalaticus* (OXI) grown in Oxalate

AN organism growing on oxalate as sole source of carbon and of energy must possess biosynthetic pathways capable of transforming this compound into all its various cell constituents. It has been suggested[1] that it might do this by oxidizing the oxalate to carbon dioxide, followed by fixation of the latter in a similar manner to that of a chemosynthetic autotroph[2]. However, it has recently been found[3] that a key enzyme of the carbon dioxide fixation cycle of autotrophs, carboxydismutase, is not synthesized by *Ps. oxalaticus* during growth on oxalate; also, carbon dioxide is not appreciably incorporated into phosphorylated compounds by such cultures. These findings eliminate the operation of an autotrophic type of metabolism and suggest that biosynthesis of cell constituents from oxalate conforms with that occurring with C_2-compounds other than acetate (see first communication). The present communication presents results indicating that incorporation of oxalate follows a similar route to that suggested for other pseudomonad species growing on glycollate (first communication) or glycine (second communication). The essential difference lies in the reduction of oxalate to glyoxylate, the latter compound being the first common intermediary metabolite of these three growth substrates.

Growing cultures of *Ps. oxalaticus* were incubated with [^{14}C] oxalate and the course of entry of the isotopic carbon into the cells was followed by chromatographic and radioautographic techniques already described[4,5]. The large amount of residual radioactive oxalate, which obscured the area of the chromatogram in which many phosphorylated compounds are found, was removed by incubating the aqueous eluates of such areas with oxalate decarboxylase obtained from *Collybia velutipes*[6]. This enzyme specifically decarboxylates oxalate to formate and carbon dioxide, both of which were easily removed on further chromatography. The results of this analysis are shown in Fig. 1, the percentages of the total radioactivity on each chromatogram that were contained in the separated compounds being plotted as functions of time. The only labelled compounds formed in 3 sec. and isolated under these conditions were glycine and phosphoglycerate. During the incubation period of 3–10 sec., the percentage of radioactivity contained in glycine diminished, while that in phosphoglycerate increased. This shows that isotope from oxalate enters glycine first and then phosphoglycerate, other metabolites such as sugar phosphates and alanine become labelled later. The following work with cell-free extracts indicates the possible nature of these initial transformations.

Crude, cell-free extracts prepared from the organism catalyse a rapid anaerobic decarboxylation of glyoxylate in which one mole of carbon dioxide is formed from two of glyoxylate. Using [^{14}C] glyoxylate

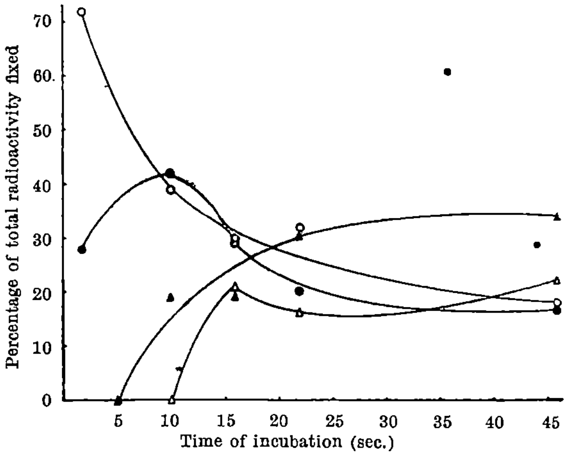

Fig. 1. Incorporation of [^{14}C] oxalate by *Ps. oxalaticus* grown in oxalate. Percentage of the total radioactivity present on each chromatogram that was contained in the separated compounds, plotted against time of incubation: ○—○, glycine; ●—●, phosphoglycerate; △—△, alanine; ▲—▲, sugar phosphates

(10^4 counts/min., under the conditions of radioassay used), and analysing the reaction products by chromatography and radioautography, the formation of radioactive glycerate (2,380 counts/min.) has been found after 15 min. anaerobic incubation, the yield of glycerate was increased almost three-fold by the addition of reduced diphosphopyridine nucleotide. No other radioactive product was found. These reactions are similar to those found in the pseudomonads grown in glycollate (first communication) and postulated in pseudomonads grown in glycine (second communication), and demonstrate a reductive conversion of glyoxylate to glycerate. The formation of some glycerate in the absence of added reduced diphosphopyridine nucleotide is probably due to endogenous reduced diphosphopyridine nucleotide present under the anaerobic conditions.

Formation of [^{14}C] glycerate (710 counts/min) was also observed in these extracts from [^{14}C] oxalate (2×10^4 counts/min.) in the presence of acetyl coenzyme A and reduced diphosphopyridine nucleotide. No other product was found on the chromatograms. Addition of these co-factors separately resulted in little synthesis of glycerate (less than 160 counts/min.).

These results indicate that the following reactions may occur in the crude extract, under the test conditions:

(i) $2 \text{ oxalate} + 2 \text{ acetyl CoA} \rightarrow 2 \text{ oxalyl CoA} + 2 \text{ acetate}$;

(ii) $2 \text{ oxalyl CoA} + 2 \text{ DPNH}_2 \rightarrow 2 \text{ glyoxylate} + 2 \text{ CoA} + 2 \text{ DPN}$;

(iii) $2 \text{ glyoxylate} + \text{DPNH}_2 \rightarrow \text{glycerate} + \text{CO}_2 + \text{DPN}$

Reaction (i), involving an acetyl coenzyme A transphorase, would lead to oxalyl coenzyme A, evidence for the existence of which has previously been presented[7].

The reduction of an acyl coenzyme A grouping to an aldehyde grouping, as suggested in reaction ii, has already been demonstrated[8] in extracts of *E. coli* with acetyl coenzyme A:

$$\text{acetyl CoA} + \text{DPNH}_2 \rightarrow \text{acetaldehyde} + \text{CoA} + \text{DPN}$$

The overall effect of the reactions would be reductively to condense oxalate to glycerate and carbon dioxide.

Under the conditions of chromatography used in the whole-cell experiments, the presence of glyoxylate, the first labelled compound to be made from the activated oxalate in reaction ii, would not be observed. However, transamination reactions leading to [^{14}C] glycine formation would reflect the presence of [^{14}C] glyoxylate. The behaviour of tartronic acid semialdehyde (the postulated intermediate (preceding communications) in reaction iii) under the conditions of chromatography are not known. The presence of a glyceric acid kinase, as in the glycollate-grown *Pseudomonas ovalis* Chester (see first communication), could lead to the early formation of radioactive phosphoglycerate from glycerate, the product of reaction iii. The appearance thereafter of isotope in sugar phosphates, alanine and C_4-compounds could then be expected from established metabolic pathways.

Full details of this work will be published elsewhere.

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CONSTITUENTS OF HUMAN HÆMOGLOBIN

Separation of the Peptide Chains of Human Globin

Schroeder and his colleagues[1] reported that human hæmoglobin is composed of four polypeptide chains of two different kinds, now referred to as α- and β-chains. Since human hæmoglobin has two identical half-molecules, each half-molecule contains one α- and one β-chain. It was of interest to separate these two different polypeptide chains and to find the distribution between them of tryptic peptides 4, 23 and 26 (ref. 2) which contain the changes in amino-acid sequence associated with the abnormal human hæmoglobins S (ref. 3) and C (ref. 4), D_α (ref. 5) and I (ref. 6), and D_β (ref. 5) and E (ref. 7), respectively (Table 3).

Itano and Singer have shown[8] that human hæmoglobin splits into two *unequal* half-molecules during dissociation at *p*H 4·3. Presumably, there are units in the hæmoglobin molecule which can be represented by αα and ββ. By an ingenious experiment using this type of reversible dissociation, Vinograd, Hutchinson and Schroeder[9] were able to show that in a mixture of hæmoglobins A and S, the αα half-molecule is interchangeable, whereas the ββ one is not. These authors argued that the β-chain in hæmoglobin S is therefore different and that it carries the mutational change associated with hæmoglobin S. Their findings are confirmed by the experiments to be presented in this article, in the course of which the α- and β-chains themselves were prepared and examined.

The splitting of horse hæmoglobin was well demonstrated by Reichmann and Colvin[10], who calculated from physical studies that the molecule is composed of four chains, of two different kinds. By prolonged boundary electrophoresis at very low *p*H, these different polypeptide chains were separated. Indications of the presence of four sub-units had previously been obtained by osmometry in strong salt solutions of both horse and human hæmoglobins[11]. In the present work, the initial experiments with human globin and hæmoglobin were modelled on Reichmann and Colvin's procedure. Whereas their method gave us results with horse globin which were similar to those published by these authors, all attempts failed to obtain indications of splitting of the human globin at low *p*H values. Further attempts were based on the experiences of Brand and Johnson[12], who were able to dissociate the seed protein legumin into about six similar sub-units by the action at alkaline *p*H of sodium dodecylsulphate.

The first positive indications that human hæmoglobin could be broken down to single chains came when human hæmoglobin A treated with sodium dodecylsulphate was examined in the ultracentrifuge at room temperature and *p*H 8·6. A single, symmetrical peak was seen, but the uncorrected sedimentation constant of $2 \cdot 0 \times 10^{-13}$ agreed reasonably well with a constant for sperm whale myoglobin (molecular weight 17,000) of $2 \cdot 3 \times 10^{-13}$ (uncorrected) obtained under identical conditions. These findings indicated that under these conditions such a hæmoglobin molecule was breaking down into quarter units, that is, into four polypeptide chains, the number expected from the analysis of the N-terminal amino-acids[1]. The corrected sedimentation constants (Table 1) are rather higher than might have been expected for quarter sub-units, no doubt due to the combination with rather large amounts of sodium dodecylsulphate. Boundary electrophoresis at 0·9° C. (Fig. 1) revealed two well-defined components in the ascending limb, although the boundaries on the descending side were not so well resolved. The final composition of this solution was: protein, 2·2 per cent; veronal, 0·12 *M*; sodium dodecylsulphate, 0·026 *M*; 0·36 gm. of sodium dodecylsulphate per gm. protein. This solution was dialysed in the cold against 43 volumes of 0·12 *M* veronal buffer, *p*H 8·6, overnight before electrophoresis.

Boundary electrophoresis in the Perkin–Elmer model 38*A* apparatus with continuous compensation produced milligram quantities of one of the two components as shown in Fig. 1. After some 24 hr. the 'fast' component or chain was removed from the cell and dialysed exhaustively against cold water before lyophilization.

Such a separation was quite reproducible, although there are reasons for believing that the exact proportion of sodium dodecylsulphate is critical. The method is also effective when hæmoglobin itself is used. Here, however, the two chains have slightly higher mobilities (see Table 1) due no doubt to the additional negative charges of the hæm groups.

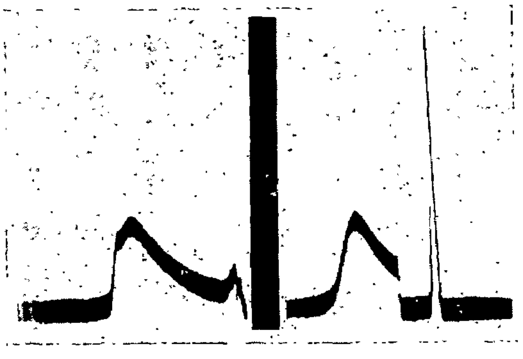

Fig. 1. Electrophoresis of human globin with sodium dodecylsulphate in veronal buffer, *p*H 8·6, ionic strength 0·12. Ascending limb on the right

Table 1. Behaviour of Globin and Hæmoglobin in the Presence of Sodium Dodecylsulphate

	Globin–sodium dodecylsulphate	Hæmoglobin–sodium dodecylsulphate
Electrophoretic mobilities		
'Fast' chain (β)	$10 \cdot 7 \times 10^{-5}$ cm.^{1} sec.$^{-1}$ V.$^{-1}$	$12 \cdot 7 \times 10^{-6}$ cm.^{2} sec.$^{-1}$ V.$^{-1}$
'Slow' chain (α)	$9 \cdot 6 \times 10^{-5}$ cm.^{3} sec.$^{-1}$ V.$^{-1}$	$11 \cdot 3 \times 10^{-5}$ cm.^{2} sec.$^{-1}$ V.$^{-1}$
Sedimentation constant (corrected S_{20})	$2 \cdot 40 \times 10^{-13}$	$2 \cdot 20 \times 10^{-13}$

Protein concentration = 2·2 per cent.

Samples of the 'fast' chain have been subjected to tryptic digestion by the methods previously described[2], although with the help of a Jacobsen-Leonis *p*H-stat[13]. Comparison of fingerprints from such digests with those of ordinary hæmoglobin digests and of digests of globin which had been treated with sodium dodecylsulphate and dialysed, showed that approximately half the usual tryptic peptides were absent. This was confirmed by the examination of tryptic peptides using one-dimensional paper electrophoresis at *p*H 6·4 (ref. 2) followed by development with ninhydrin and with reagents specific for the amino-acids histidine, tyrosine, arginine and tryptophan[14]. There was a little doubt about the presence or absence in the 'fast' chain of a few peptides, but it was clear that peptide 26 (hæmoglobin E and D_{β} changes) is present, whereas peptide 23 (hæmoglobin D_{α} and I changes) is absent and must be on the 'slow' chain. Peptide 4 (hæmoglobin S and C changes) is present, as was shown by electrophoresis at *p*H 3·6 of the band of neutral peptides obtained at *p*H 6·4, followed by a qualitative analysis of the amino-acid composition of the peptide containing histidine. Hence peptides 4 and 26 are on the 'fast' chain and peptide 23 is presumably on the 'slow' chain.

These findings confirm Schroeder's conclusion about the presence of two types of polypeptide chain in human hæmoglobin. Further experiments showed that the 'fast' chain is the β-chain, and not the α-chain as provisionally indicated[15].

In order to obtain a clearer picture of the distribution of the tryptic peptides between the α- and the β-chain, it was clearly desirable to prepare both chains and to identify them. Wilson and Smith[16] have worked out three ways of obtaining pure samples of the two different polypeptide chains of horse globin. They use preparative boundary electrophoresis at low *p*H, fractional precipitation with acid/acetone and ion exchange chromatography in a urea gradient. The last method was used, without modification, in the present experiments with globin from human hæmoglobin A. Whole globin was fractionated on an 'Amberlite IRC-50/XE 64' or 'CG 50' type 2 column with a urea gradient[16] of 2 *M*–8 *M*, always adjusted to *p*H 1·9 with hydrochloric acid. As Fig. 2 shows, two peaks are obtained, representing the α- and the β-chain, in that order, although the separation is poorer than that obtained by Wilson and Smith for horse globin. It was to be expected from their behaviour in boundary electrophoresis that the human globin chains would be more difficult to separate on an ion-exchange column. No doubt the method could be adapted to suit human globin better than it does at present. Wilson and Smith found three peaks in the case of horse globin, peaks 2 and 3 both having the same N-terminal dipeptide, namely, valyl-glutamyl-. The reason for the doubled peaks could be association of the molecules of this chain—shown by these chains in solution—or it could be connected with the fact that horse hæmoglobin usually shows two electrophoretic components. If the latter explanation be correct, then this electrophoretic difference can be assumed to reside in the polypeptide chain of horse globin which begins with valyl-glutamyl-. Since all carboxyl groups are uncharged at such a low *p*H, the difference would probably involve the basic amino-acids of this chain.

The chains were obtained by dialysis and freeze drying. In part they were digested with trypsin after heat denaturation. Examination of such digests by fingerprinting[2] and by one-dimensional ionophoresis at *p*H 6·4[2] showed that the known tryptic peptides are fairly evenly distributed between the two fractions (Fig. 3). The investigation of some of these peptides is still proceeding. By the methods used in the investigation of the human hæmoglobins 'D' (ref. 5)—particularly by specific staining reactions—it was possible to show that peptide 23 and peptide 26 occurred in the fractions I and II, respectively. This is interesting, because peptide 23 is involved in the mutations which result in hæmoglobins I and D_α and peptide 26 in hæmoglobins E and D_β. The location of peptide 4 (hæmoglobins S and C mutations) was not immediately apparent, because in hæmoglobin A this peptide is one of several uncharged peptides at the *p*H used for the ionophoresis, namely, 6·4. However, when the neutral peptides from digests of the two chains were compared by ionophoresis at *p*H 3·6, it became clear that peptide 4 is part of the chain in fraction II, namely, the β-chain (Fig. 3). This is in agreement with Vinograd and Schroeder's findings[9].

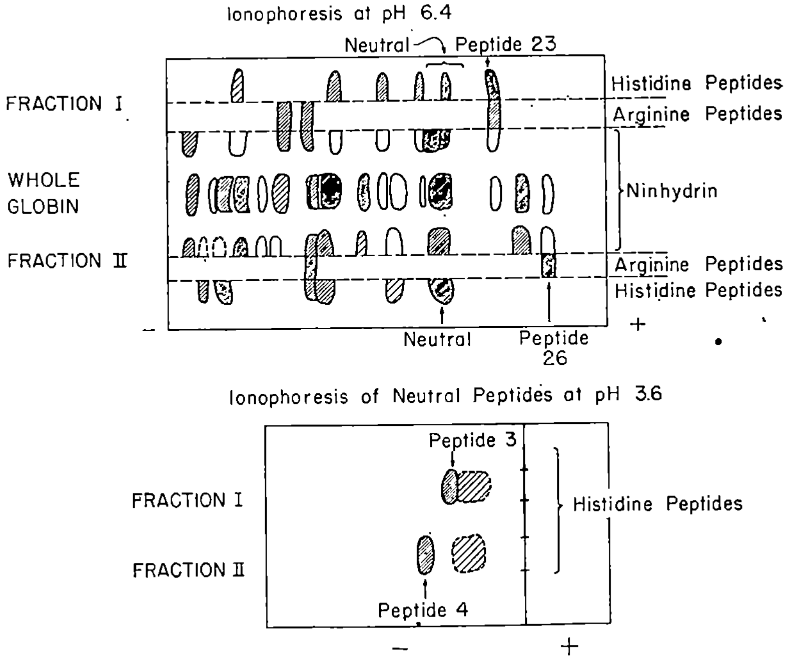

Fig. 3. Tracings of ionograms of tryptic digests; ionophoresis at *p*H 6·4. Colour reactions for specific amino-acids as in ref. 14

In order to identify fractions I and II with Schroeder's α- and β-chain, each fraction as well as whole globin were subjected to degradation from the amino-end with Fraenkel-Conrat's paper strip modification[17] of the Edman method. Table 2 shows that fraction I begins with valyl-leucine and is therefore the α-chain, whereas II begins with valyl-histidine- and is the β-chain. Table 3 indicates the distribution of the peptides carrying the various mutational alterations.

These results have interesting genetic implications[15]. The findings of the amino-acid changes in hæmoglobins S, C and E support the widely accepted hypothesis of a correlation between the linear fine-structure of the polypeptide chain controlled by that gene. When discussing a protein such as human hæmoglobin, which has two kinds of peptide chains, one is tempted to extend these ideas in the following way: suppose that there are two hæmoglobin genes; an 'α-chain gene' to control the amino-acid sequence of the α-peptide chain, and a 'β-chain gene'. Mutations may affect one or the other of these genes; for

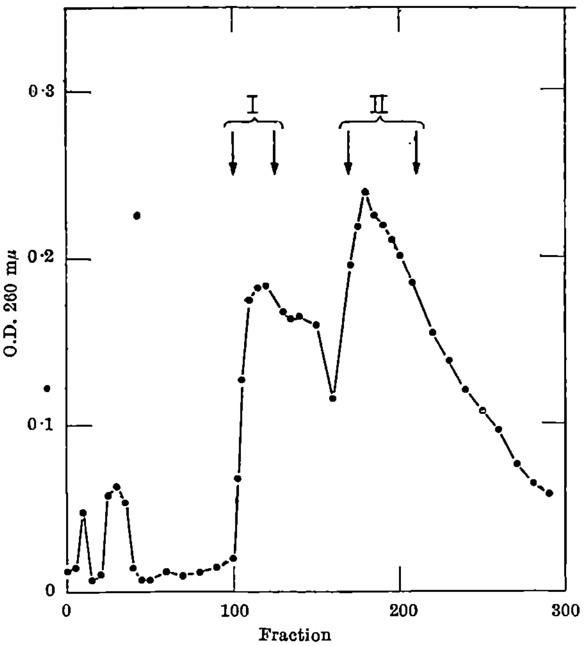

Fig. 2. Chromatography of human globin in a gradient of urea (see text for details)

Table 2

Schroeder's nomenclature of chains (ref. 1)	Whole globin*	Fraction I	Fraction II
	$\alpha + \beta$	α	β
Edman degradation (ref. 17)			
Step 1	Valine+++	Valine++	Valine++
Step 2	Leucine++	Leucine++	Leucine trace
(acid extract)	Histidine+	Histidine trace	Histidine+
(basic extract)	Histidine++	Histidine trace	Histidine++
N-terminal sequence	val-leu- val-his-	val-leu	val-his

* Double quantity.

Table 3

Hæmoglobin types		Peptide in which change takes place
	α-Peptide chain	
Hb-D_{α}, Hb-I		23
	β-Peptide chain	
Hb-S, Hb-C		4
Hb-D_{β}, Hb-E		26

example, the hæmoglobin S, C, D_{β} and E mutations would, in this picture, be expected to occur on the β-chain gene, whereas, for example, the hæmoglobin D_{α} and I changes would occur as the result of alteration on the α-chain gene. Moreover, the loci of the two mutations of the α-chain gene would be expected to be very close together, since they effect changes within the same small peptide. The loci of the four β-chain mutations would in this formulation be found in two pairs—hæmoglobins D_{β} and E close together and hæmoglobins S and C in the identical location[4].

The possibility that there might be two hæmoglobin genes was put forward by Neel and his colleagues[18] in order to explain the pattern of inheritance of both hæmoglobin S and hæmoglobin G in one family. It has also been proposed by Smith and Torbert in connexion with a family tree involving hæmoglobin 'Hopkins 2' (ref. 19). The present results, the assignment of chemical alterations to one or other of the two peptide chains, enable us to present a more detailed and more convincing picture of the gene-protein relationship in the hæmoglobins.

I wish to thank Dr. D. B. Smith and Dr. J. Vinograd for their courtesy in allowing me to see copies of their papers prior to publication. Thanks are also due to Dr. P. Johnson, of Cambridge, for many helpful discussions. The expert assistance of Mrs. R. Fishpool and Miss E. Sullivan is gratefully acknowledged, as is the help given by Mr. Boon, of the Biochemical Laboratory, Cambridge, who carried out the ultracentrifuge determinations. This work was supported in part by a grant from the Medical Foundation, Inc., Boston, the help of which is gratefully acknowledged.

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Comparison of Normal Adult Human Hæmoglobin with Hæmoglobin I by 'Fingerprinting'

ACCORDING to Rucknagel *et al.*[1] the occurrence of hæmoglobin I is genetically determined but does not appear to cause a severe anæmia. It has a lower isoelectric point than the normal hæmoglobin (hæmoglobin-A) in a moving-boundary electrophoresis experiment, and migrates more rapidly in alkaline buffers and less rapidly in acid buffers ; the electrophoretic mobility differences[2] between hæmoglobins A and I are 0·6 to 0·7 × 10^{-5} cm^2. $sec.^{-1}V.^{-1}$. We wish to report that in hæmoglobin I a mutational alteration is found in tryptic peptide 23 (ref. 3), the peptide which also contains the change[4] associated with hæmoglobin D_{α}. The other peptides appear to be normal. In hæmoglobins S and C, tryptic peptide 4 is altered[5,6] and tryptic peptide 26 in hæmoglobins E (ref. 7), and D_{β} (ref. 4). Therefore, we know of at least three parts of the molecule which undergo changes due to mutation in the gene or genes which control the biosynthesis of the hæmoglobin molecule.

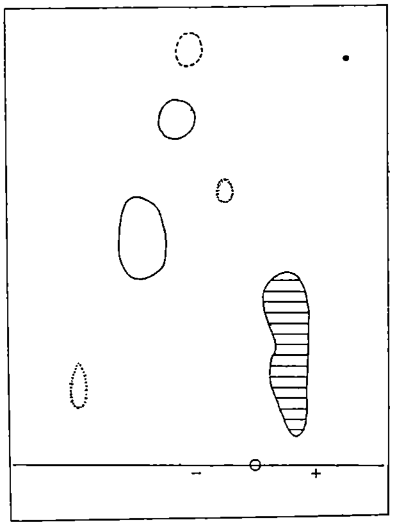

Fig. 1. Tracing of 'fingerprint' (ref. 3) of the tryptic digest from hæmoglobn I developed for tryptophan-containing peptides (ref. 10). The area of peptide 23 is cross-hatched, indicating a positive reaction for tryptophan, whereas peptide 23 of hæmoglobin A is negative. Electrophoresis was carried out at *p*H 6·4 in the horizontal direction and subsequent chromatography in butanol/acetic acid in the vertical direction (ref. 3)

The blood specimen was made available by Dr. Tocantins from a patient (J. W.) with hæmoglobin A-I and whose red cells sickled under certain conditions[8]. Hæmoglobin I was separated by means of the starch block electrophoresis technique of Kunkel[9]. 'Purified' hæmoglobin I was denatured by heat and digested with trypsin[3], and from it was obtained a mixture of peptides for examination by 'fingerprinting'.

Such a 'fingerprint' revealed that peptide 23 of this hæmoglobin moved more rapidly towards the anode than the normal peptide, in line with peptides 24 and 25. A specific colour reaction[10] (Ehrlich's reagent) on a 'fingerprint' revealed that peptide 23 of hæmoglobin I contains tryptophan whereas the corresponding one in hæmoglobin A does not (Fig. 1). In a one-dimensional paper electrophoresis it is possible to demonstrate the new tryptophan-containing peptide under an ultra-violet lamp. It is not yet clear whether other amino-acids in peptide 23 are involved in the change. The specific colour reactions[10] carried out directly on the ionogram revealed the presence of arginine, tyrosine, and histidine (Fig. 2) which also occur in peptide 23 of normal hæmoglobin. It is hoped that further experiments will reveal in detail the change undergone by peptide 23.

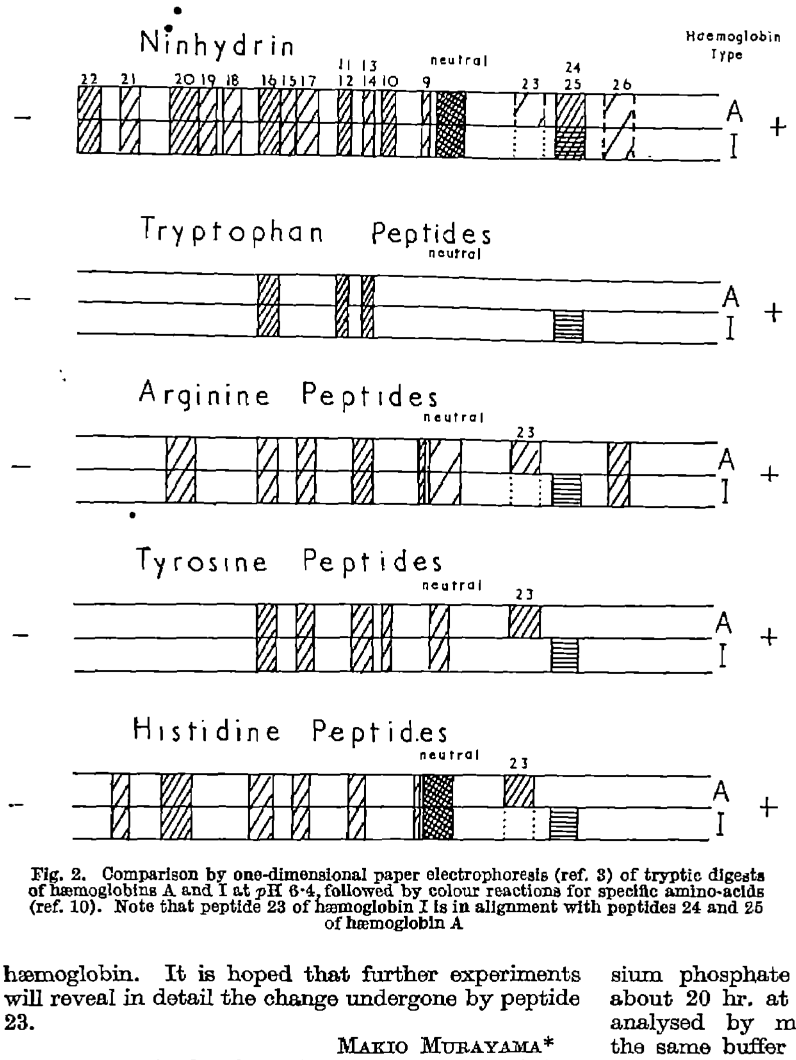

Fig. 2. Comparison by one-dimensional paper electrophoresis (ref. 3) of tryptic digests of hæmoglobins A and I at pH 6·4, followed by colour reactions for specific amino-acids (ref. 10). Note that peptide 23 of hæmoglobin I is in alignment with peptides 24 and 25 of hæmoglobin A

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Formation of Normal and Doubly Abnormal Hæmoglobins by Recombination of Hæmoglobin I with S and C

A MOLECULE of normal human adult hæmoglobin (hæmoglobin A) is symmetrical about a dyad axis[1] and is composed of four hæm groups and four polypeptide chains, a pair of α-chains and a pair of β-chains[2]. Hæmoglobins A, S, and C dissociate asymmetrically in acid into two unlike sub-units, each of which consists of a pair of identical chains and two hæms[3,4]. Complete molecules are regenerated from these sub-units when an acidified solution is neutralized, and sub-units are exchanged when a mixture of a pair of unlike hæmoglobins is dissociated and recombined. The chemical abnormalities of hæmoglobins S and C occur at the same place in the β-chain[5,6]. Hæmoglobin I, on the other hand, is abnormal in the α-chain[7]. We wish to report evidence for the formation of hæmoglobin A and a doubly abnormal molecule when hæmoglobin I is recombined with hæmoglobin S or C.

A mixture of hæmoglobins A and I received from Dr. L. M. Tocantins was used[8]. The mixture, and mixtures of it with hæmoglobin S and with hæmoglobin C, were examined electrophoretically both before and after recombination. All samples were in the form of carbonmonoxyhæmoglobin. Recombined mixtures were prepared by dissociation in acetate-sodium chloride buffer of pH 4·7, Γ/2 0·2 (ref. 4) for 4 hr. at 5° C. followed by dialysis against potassium phosphate buffer of pH 6·3, Γ/2 0·02, for about 20 hr. at 5° C. The resulting samples were analysed by moving-boundary electrophoresis in the same buffer for 5 hr. at 3° C. with a potential gradient of 8·5 V. cm.$^{-1}$. Control electrophoretic analyses on undissociated aliquots of the same mixtures were carried out under identical conditions. Satisfactory resolution was obtained only in the ascending limb. When a mixture of carbonmonoxyhæmoglobins A, I and S was recombined, a new component appeared between A and I. At the same time the proportion of hæmoglobin A increased and the proportions of I and S decreased. Recombination of carbonmonoxyhæmoglobins A, I and C produced no new electrophoretic component; however, the proportion of hæmoglobin A increased with decrease of I and C. No new component or change in proportions occurred when carbonmonoxyhæmoglobins A and I were recombined. The results are shown in Fig. 1 and Table 1. The numerical values of Table 1 are directly proportional to the areas under the peaks of Fig. 1. These areas are probably anomalous because of low ionic strength of buffer. However, since aliquots of the same mixture were used in each pair of analyses, change in relative areas following recombination must reflect change in true composition.

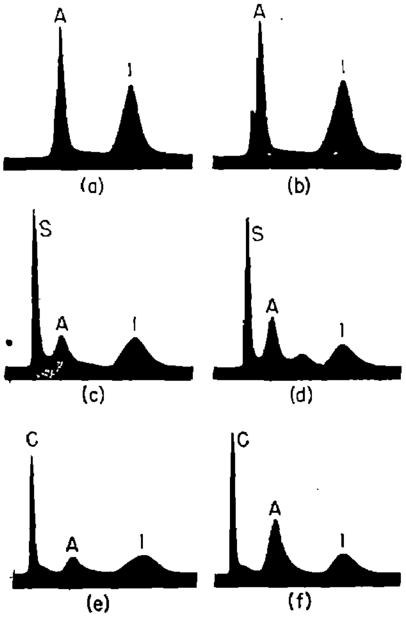

Fig. 1. Ascending boundary patterns from electrophoresis of 1·0 per cent carbonmonoxyhæmoglobin in phosphate buffer of *p*H 6·3, Γ/2 = 0·02. The direction of migration is from right to left. From left to right the components are: (*a*) A, I control; (*b*) A, I recombined; (*c*) S, A, I control; (*d*) S, A, I recombined. Note the new component ($s_2i_2^{-2}$) between A and I and the increase in proportion of A; (*e*) C, A, I control; (*f*) C, A, I recombined. Note the increase in the proportion of A ($a_2u_2 + c_2i_2$)

A simplified nomenclature[3,4] is convenient for discussion of dissociation-recombination phenomena. The β-chains of hæmoglobins A, S and C are *a*, *s* and *c*, respectively; and their common α-chain is *u*. The abnormal α-chain of hæmoglobin I is *i*, and its β-chain, presumably normal, is *a*. The abnormalities in net charge of hæmoglobins S and C are + 2 and + 4, respectively[5]. The mobility of hæmoglobin I indicates an abnormality in net charge of close to − 4. The net charge of the unaltered portions of the molecules may be omitted in the present discussion; accordingly carbonmonoxyhæmoglobins A, S, C and I may be written a_2u_2, $s_2u_2^{+2}$, $c_2u_2^{+4}$, and $a_2i_2^{-4}$, respectively. Asymmetric dissociation would result in the sub-units a_2, s_2^{+2}, c_2^{+4}, u_2, and i_2^{-4}.

We can now interpret our results with the assumption of asymmetrical dissociation and recombination. When a mixture of a_2u_2 and $a_2i_2^{-4}$ is recombined, exchange of a_2 sub-units can occur without effect on electrophoretic composition, in agreement with our observations on the mixture of carbonmonoxyhæmoglobins A and I. The situation is analogous to the exchange of u_2 sub-units when mixtures of carbonmonoxyhæmoglobins A, S and C were recombined. Recombined mixtures yielded the same electrophoretic patterns as corresponding untreated mixtures, and exchange was demonstrated by use of labelled molecules[3,4]. Since recombination of carbonmonoxyhæmoglobin A with S, C or I is not associated with change in composition, it appears that the effects observed in the mixture A, S and I, and in the mixture A, C and I, arise from recombination of S and C, respectively, with I. Asymmetrical recombination of $s_2u_2^{+2}$ and $a_2i_2^{-4}$ would result in a mixture of a_2u_2, $s_2i_2^{-2}$, and the original components. The net effect on the composition of a mixture of carbonmonoxyhæmoglobins A, S and I would be the appearance of a new component between A and I, increase in A and decrease in S and I. Asymmetrical recombination of $c_2u_2^{+4}$ and $a_2i_2^{-4}$ would produce a mixture of a_2u_2, c_2i_2, and the original components. Since c_2i_2 has the same net charge as a_2u_2, no new component would be detected. The effect on a mixture of carbonmonoxyhæmoglobins A, C and I would be an increase in the A component, which includes both a_2u_2 and c_2i_2, and decrease in C and I.

Table 1. COMPOSITION OF HÆMOGLOBIN MIXTURES BEFORE AND AFTER RECOMBINATION

Mixture		Electrophoretic composition: per cent of total $a_2i_2^{-4}$ (I)	$s_2i_2^{-2}$	a_2u_2 (A)	$s_2u_2^{+2}$ (S)	$c_2u_2^{+4}$ (C)
A+I	Control	53	—	47*	—	—
	Recombined	55	—	45*	—	—
A+I+S	Control	34	—	24*	42	—
	Recombined	23	11	32	34	—
A+I+C	Control†	36	—	20	—	44*
	Recombined	22	—	42‡	—	36*

* Includes 3–4 per cent of trailing shoulder.

† Re-run of original control; C peak too sharp in original for determination of area.

‡ Probably includes c_2i_2.

Thus our observations are consistent with the assumption of asymmetrical recombination between carbonmonoxyhæmoglobin I, which is abnormal in the α-chain, and carbomonoxyhæmoglobin S or C, which is abnormal in the β-chain, to produce carbonmonoxyhæmoglobin A and a carbonmonoxyhæmoglobin molecule composed of two different pairs of abnormal chains. According to these results, it is possible for an individual who is heterozygous for an abnormality in each chain to have four molecular species of adult hæmoglobin in his red cells, provided the two types of chains are physically independent up to the time they associate to form complete molecules. If the abnormalities in net charge of the two abnormal chains are equal and opposite, the four species would appear as three electrophoretic components. In either circumstance one of the four species would be composed entirely of normal chains. Formation of a normal protein molecule by association of the normal components of two different abnormal molecules suggests one possible mechanism for extranuclear formation of a normal enzyme molecule by the co-operative action of two mutant strains of the same organism, neither of which produces active enzyme[4].

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LETTERS TO THE EDITORS

PHYSICAL SCIENCES

Spectrum and Structure of the Free Methylene Radical

SEVENTEEN years ago, one of us[1] suggested that the so-called λ4050 group observed in comets was due to the free methylene radical (CH_2). This suggestion was not confirmed by later experiments[2-4]. Ever since the original misidentification of the 4050 group, experiments have been proceeding in this laboratory with the aim of finding the true spectrum of CH_2. However, it was only at the end of last year that some promising features were observed near 1400 A. in the flash photolysis of diazomethane. Recently, one of these features has been positively identified as due to free CH_2.

In the first order of our 3-m. vacuum spectrograph the group of features under consideration consists of six slightly diffuse 'lines' which show, on substitution with deuterium, a marked shift, thus establishing that the carrier of this group must contain one or more hydrogen atoms. The strongest feature in this group occurs in the flash photolysis of ordinary diazomethane at 1414·5 A., in fully deuterated diazomethane at 1415·8 A. When partly deuterated diazomethane is used, a third feature is observed at 1415·5 A. In this way it is shown that there are two hydrogen atoms present in the molecule responsible for this spectrum. While this made it very likely that CH_2, CHD and CD_2 are responsible for the observed spectra, conclusive proof could only be obtained by a study of the rotational fine structure of some of the features observed.

Unfortunately, it turned out that in the fourth order of our vacuum spectrograph all the features observed in the flash photolysis of ordinary diazomethane were rather diffuse. However, in observing the corresponding spectrum in deuterated diazomethane, it was found that the principal feature at 1416 A. did show a rather well-resolved fine structure. This difference between the deuterated and non-deuterated molecule is very similar to the condition found[5] for the 2160 A. band of CH_3 and CD_3, and is apparently due to the fact that a deuterated molecule predissociates much less easily than a non-deuterated molecule.

The fine structure of the 1415·8 A. feature in the deuterated molecule consists of a simple *P*- and *R*-branch, each of which shows a clear alternation of intensity. The presence of this alternation proves beyond doubt that there must be two symmetrically placed identical atoms (deuterium atoms) in the molecule. The absence of a *Q*-branch proves that this is either a parallel band of a linear molecule or the $K = 0$ sub-band of a parallel band of a (nearly) symmetrical top molecule such that rotation about an axis perpendicular to the figure axis exchanges the deuterium atoms. Further confirmation was obtained by the observation of a similar band without an alternation of intensity in the flash photolysis of partly deuterated diazomethane. The spacing of the lines in the fine structure of the bands in the fully deuterated and partly deuterated compounds supplies values for the rotational constants (reciprocal moments of inertia) in the upper and lower states of the two molecules involved. These values are:

$$B'(CD_2) = 3{\cdot}59_5 \qquad B''(CD_2) = 3{\cdot}95_0 \text{ cm.}^{-1}$$
$$B'(CHD) = 4{\cdot}80_8 \qquad B''(CHD) = 5{\cdot}33_3 \text{ cm.}^{-1}$$

The magnitudes of these rotational constants are compatible only with the assumption that the molecule involved is of the type XD_2 and XHD respectively. From the method of production of the spectrum it appears impossible that X can be anything but C (carbon). The ground-state and first excited state of NH_2 are known, and definitely are not involved in the bands under investigation. Moreover, both the well-known spectra of ND_2 and ND in the visible and in the ultra-violet regions are absent, while the spectrum of CD (and CH) is very prominent. Thus we consider the identification of the carrier of the spectrum as free methylene as established.

The simplest and most obvious interpretation of the observed fine structure would appear to be that the molecule is linear in both the upper and lower states of the transition. With this assumption one obtains two independent values for the CH (or CD) distance from the rotational constants of B'' of CD_2 and CHD, namely:

$$r_0'' = 1{\cdot}029 \text{ and } 1{\cdot}034 \text{ A.}$$

The slight difference could be accounted for by the effects of zero-point vibration.

If, on the other hand, one assumes the molecule to be non-linear and uses the two moments of inertia to determine the two structural parameters r_0'' and ∠HCH one finds:

$$r_0'' = 1{\cdot}071 \text{ A. and } \angle HCH = 140^\circ.$$

However, these results imply that the rotational constant $A''(CD_2)$ would be 41·7 cm.$^{-1}$ and therefore several other sub-bands with $K = 1, 2, 3, \ldots$ would be expected, for which no evidence has been found. The absence of these sub-bands could be accounted for if it is assumed that the upper state is linear or that levels with $K \neq 0$ in the upper state are strongly predissociated and therefore escape observation. On account of the effect of zero-point vibration, a definite decision between the linear and non-linear structure of the molecule in the ground-state is not yet possible. All one can say definitely at this moment is that the HCH angle is between 140° and 180°.

The fact that in CD_2 the strong lines are those of odd J indicates that the lower electronic state of the transition is not totally symmetrical. Indeed, for linear CH_2 the predicted[6] ground-state is readily seen to be $^3\Sigma_g^-$, which would lead exactly to the observed intensity alternation. It is conceivable that the lower state of the transition, even though it has been observed in absorption, is not the ground-state of the molecule, but this would entail the assumption that the molecule can survive up to 5,000 collisions with the inert gas molecules present before going over to the real ground-state.

While the question of the ground-state still remains to be settled, we believe that it has been definitely established that the spectrum under consideration is due to the free methylene radical and that in the lower state of the observed transition the molecule has an HCH angle between 140° and 180° and a non-totally symmetrical electronic structure. The life-time of the CH_2 radical under the conditions of our experiment (partial pressure of diazomethane before photolysis 0·02 mm., partial pressure of inert gas 2 mm. or more) was about 15 μsec., that is, of the order of the time between collisions of CH_2 with CH_2N_2.

Many members of this laboratory have contributed to the final success of these investigations by their suggestions, critical advice and other help. To all of them we are greatly indebted.

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Removal of Dipolar Broadening of Nuclear Magnetic Resonance Spectra of Solids by Specimen Rotation

THE nuclear magnetic resonance spectrum of a solid rotated at high speed consists of a narrowed central line and a set of side-spectra spaced at integral multiples of the rotation rate of either side[1,2]. The interaction energy between each pair on nuclear magnets in the solid contains the angular factor $(3 \cos^2 \theta - 1)$, where θ is the angle between the internuclear vector and the applied field. When the solid rotates about an axis making an angle α with the applied field, the angular factor may be expressed[3] as the sum of its mean value $\frac{1}{2} (3 \cos^2 \alpha - 1) (3 \cos^2 \gamma - 1)$, where γ is the angle between the internuclear vector and the axis of rotation, and two time-dependent terms, $(3/2) \sin 2\alpha \sin 2\gamma \cos \omega_r t$ and $(3/2) \sin^2 \alpha \sin^2 \gamma \cos 2 \omega_r t$, where ω_r is the angular frequency of rotation. The two time-dependent terms lead to the formation of the side-spectra. It should be noted that when α is 90°, as in our earlier experiments[1,2], the first of these terms is absent, so that side-spectra occur in this case at even multiples of ω_r only; for general α, the side-spectra occur at odd and even multiples of ω_r. The form of the mean value of the angular factor for each nuclear pair leads to the conclusion that the central spectrum should have the shape found for the static crystal when the applied field is directed along the axis of rotation, but reduced in width by the factor $\frac{1}{2} (3 \cos^2 \alpha - 1)$, and having a second moment[4] reduced by a factor $\frac{1}{4} (3 \cos^2 \alpha - 1)^2$. Thus, in particular, when α has the value $\cos^{-1} (1/\sqrt{3}) = 54° 44'$, the dipolar broadening of the central line should be removed[5]. With a speed of rotation large compared with the static line-width, the side-spectra will be displaced far from the centre and will be weak, leaving only a sharp central line broadened by residual non-dipolar causes.

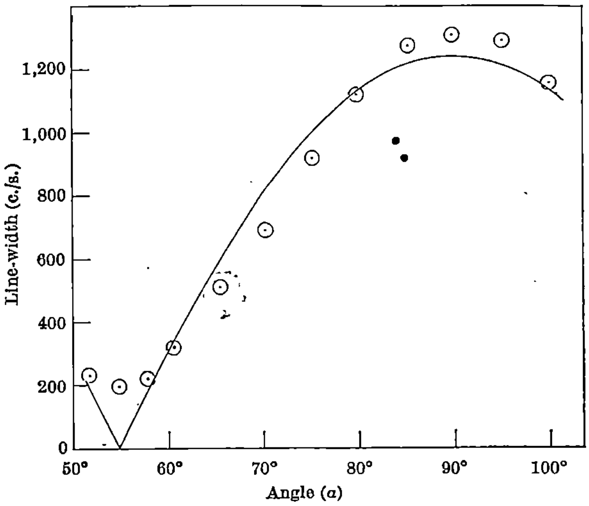

Fig. 1. Variation of line-width of the sodium-23 resonance spectrum of a rotating crystal of sodium chloride with the angle α between the axis of rotation and the direction of the applied field. The full line is the theoretical curve for a spectrum broadened solely by dipolar interactions; the circles are the experimental observations

We have extended our experiments on a rotating crystal of sodium chloride to cover a range of angles α from 50° to 100°. The axis of rotation was [001]. The measured width of the central line of the sodium-23 resonance spectrum determined between derivative maximum and minimum is plotted in Fig. 1. Also shown in Fig. 1 is the curve of $\frac{1}{2}|3 \cos^2 \alpha - 1|\delta\nu_0$, where $\delta\nu_0$ is the line-width for the static crystal with the applied field along [001]. The general agreement is quite good, but it is to be noticed that when $\alpha = 54° 44'$, the central line has a finite width of 200 c./s., which is greater than the instrumental breadth. This residual width may in this crystal arise from interactions between the electric quadrupole moments of the sodium-23 nuclei and electric field gradients caused by imperfections in the cubic crystal. The central line thus has a residual width about one-tenth of that for the static crystal, and a second moment of the order of 1 per cent of that for the static crystal. Such broadening would be difficult to detect while it is overlaid by the much larger dipolar broadening of the static crystal.

In Fig. 2 is shown the derivative spectrum for $\alpha = 54° 44'$ at a rotation rate of 810 c./s. The first three side-spectra are visible on either side. Although the rate of rotation was sufficient to separate the side spectra from each other and from the central line, it was insufficient to remove them from the scene.

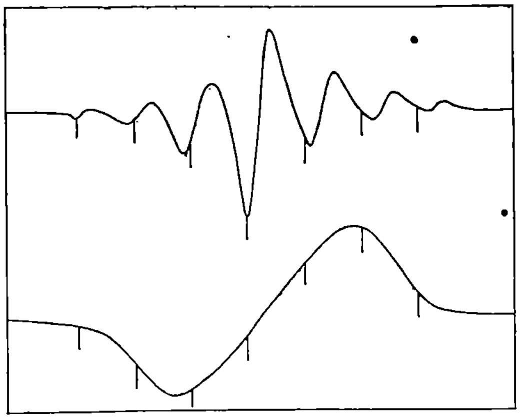

Fig. 2. The upper curve is the derivative spectrum for the crystal rotated at 810 c./s. about an axis making an angle 54° 44′ with the direction of the field. The lower curve is the derivative spectrum for the static crystal. The markers are 790 c./s. apart

Fig. 2 also shows, for comparison, a spectrum obtained when the crystal was at rest.

Several practical consequences appear to follow from the removal of dipolar broadening from the central line. In the first place, the position of the central resonance frequency can be determined with much greater precision; in our example the improvement is by a factor of ten. In this way a greater accuracy may be obtained in the measurement of nuclear magnetic moments when solid specimens are used. Secondly, the relative chemical shifts (and for metals, Knight shifts) may be determined with much greater precision. Thirdly, broadening or fine-structure caused, for example, by quadrupolar interactions, electron-coupled spin exchange or different chemical shifts on non-equivalent sites, may be revealed by the removal of the dipolar broadening which, in solids, usually masks them.

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Electron Microscopy of Oleophobic Monolayers

Oleophobic monolayers of stearic acid on mica have been studied by means of the electron microscope. Mica was chosen as the substrate because clean surfaces, which are molecularly flat over large areas, are easily obtained by cleavage. Stearic acid was retracted from a solution in hexadecane in the manner described by Bigelow, Pickett and Zisman[1] and a preshadowed carbon replica of the surface taken; 40 per cent gold/palladium was found to be the most suitable shadowing material.

Fig. 1 shows a typical result. The contrast of the micrograph is enhanced by agglomeration of the shadowing material on those parts of the surface covered by stearic acid. It will be seen that the monolayer is present in islands, which measurement of shadow-lengths show to be 25 A. thick. A close examination of the monolayer islands does in some instances show a tendency for the metal particles to arrange themselves in lines, which may suggest some regular array, within the islands, of the micelles which Epstein[2] suggests exist in monolayers.

Monolayers of stearic acid retracted from the melt[3] do not show the island structure of those retracted from hexadecane solution, so this structure cannot be attributed to evaporation of stearic acid during pumping prior to shadowing, or to bombardment of the surface by metal particles. It is evident from Fig. 1 that the surface is only partially covered by stearic acid, so it is pertinent to ask how it is that the surface is oleophobic. It is suggested that hexadecane is incorporated in the monolayer. The attractive forces between hydrocarbon chains are believed to be responsible for the orientation of long-chain polar compounds at both the solid and liquid interfaces; and Sobotka and Rosenberg[4] have shown that it is possible to spread mixed films of stearic acid and long, straight-chain hydrocarbons on water surfaces, where the hydrocarbon will not spread by itself. A similar mechanism may operate in this case. Hexadecane is able to orient itself alongside adsorbed molecules of stearic acid, and may be gradually replaced as more stearic acid diffuses to the surface.

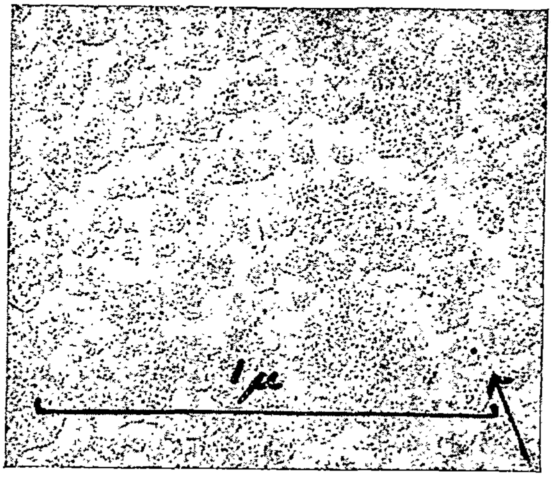

Fig. 1. Electron micrograph of a replica of a mica surface which has been dipped in a 0·1 per cent by weight solution of stearic acid in hexadecane for 30 sec. The arrow shows the direction of shadowing. The island structure of the monolayer is apparent

Although no quantitative results are available yet, it is evident from micrographs that the area covered increases with time of immersion, and with concentration of solution for a given time of immersion. Furthermore, if a monolayer is prepared by retraction of a drop on the mica surface, it is found that only a third of the surface is covered by acid. Fig. 2 shows a close-packed hexagonal arrangement of molecules where the black circles represent stearic acid and the white circles hexadecane. It can be seen that each hexadecane molecule has three stearic acid molecules among its six nearest neighbours. It is suggested that when a stearic acid molecule is adsorbed, hexadecane molecules are able to orient themselves beside it. When the condition in Fig. 2 is reached, the bulk liquid rests on an oleophobic surface of methyl groups and retracts, being unable to differentiate between the end groups of the acid and the hydrocarbon. Since the hexadecane has a much greater vapour pressure than stearic acid, it is pumped off during the preparation of the replica, and then the acid molecules collapse into islands as shown in Fig. 1. In no case has an oleophobic film been found to cover significantly less than a third of the surface.

The observations of Bigelow and Brockway[5], who find only a small reduction in contact angle when the

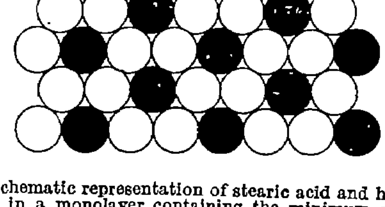

Fig. 2. Schematic representation of stearic acid and hexadecane molecules in a monolayer containing the minimum number of stearic acid molecules necessary for the surface to be oleophobic. The black circles represent stearic acid and the white hexadecane

density of adsorbed acid molecules is reduced by dipping in hexadecane, may be explained as a result of the reverse process taking place, hexadecane replacing stearic acid which has been dissolved away. These authors do point out that a surface may become oleophobic before the adsorption process is complete.

Identical observations have been made on retracted monolayers of long-chain aliphatic alcohols and primary amines. It has not been possible to observe any island structure when the mica has not been immersed in solution long enough for it to become oleophobic, although Bigelow and Brockway were able to obtain faint layer lines in electron diffraction pictures[5]. It may well be that any clusters of molecules oriented on the surface are too small to be replicated satisfactorily.

I am indebted to Dr. F. P. Bowden and Dr. D. Tabor of this Laboratory for helpful discussion, and to Joseph Lucas, Ltd., for a research grant.

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Magnetometric Titration: a New Method of Chemical Analysis

It is well known that the addition of paramagnetic solutes to water brings about a marked reduction in the nuclear spin-lattice relaxation time of solvent protons[1], the inverse of the relaxation time being linearly related to solute concentration according to the equation:

$$(T_1^{-1} - T_0^{-1}) = \alpha \mu_N^2 C$$

where T_1 and T_0 are spin-lattice relaxation times in the presence and absence of added solute, respectively; α is a proportionality constant; μ_N is a parameter expressing the effectiveness of a particular solute in this phenomenon, sometimes called the 'effective' paramagnetic moment of the solute; C is the concentration of the solute. In the case of solutions of paramagnetic complex ions, the magnitude of the effect (that is, the value of μ_N) depends on the nature of the co-ordinated groups[2]. We find that the phenomenon enables the replacement of one ligand by another in solution to be followed with sufficient precision to form the basis for a method of determining the concentration of metal ions, and it is now suggested that this method of analysis should be widely applicable in cases where the addition of a complexing agent to the solution of a paramagnetic ion in solution causes the formation of a new complex ion of different μ_N and of high stability in solution. The analyses can conveniently be carried out by use of a low-resolution nuclear magnetic-resonance spectrometer.

The application of the method to the titration of nickel(II) is illustrated in Fig. 1. The breaks in the curve correspond to equivalence points, in a manner somewhat reminiscent of conductimetric titrations. Nickel(II) represents a particularly favourable and interesting case for this method, since the diamagnetic species $[Ni(CN)_4]^{2-}$ does not catalyse the spin-lattice relaxation at all. Values of $(T_1^{-1} - T_0^{-1})$, corrected for the dilution effect which accompanies addition of titrating agent, are plotted against the amount of potassium cyanide added to an ammoniacal solution of nickel cyanide, that is, a solution of $[Ni(NH_3)_6]^{2+}$ $[Ni(CN)_4]^{2-}$.

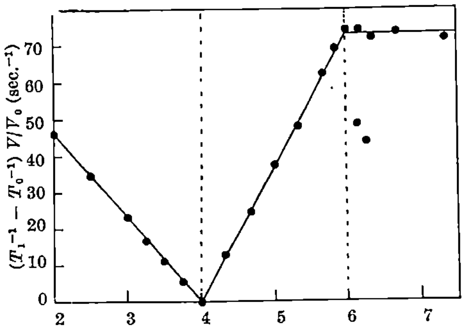

Fig. 1

The curve is interesting in that two equivalence points are observed. These occur after addition of four and six moles of cyanide per mole of nickel(II) respectively, and demonstrate the formation of stable species $Ni(CN)_4^{2-}$ and $Ni(CN)_6^{4-}$. Since present indications from other experimental methods are that $[Ni(CN)_6]^{4-}$ (in aqueous solution) is not paramagnetic, this particular result raises other problems, because only paramagnetic solutes are thought to be effective in catalysing spin-lattice relaxation.

A feature which makes the technique attractive in analytical chemistry is the small amount of solute required. In our apparatus sample volumes of 0·23 c.c. and concentrations of nickel(II) in the range 0·01–0·1 *M* were convenient, but both these values could be substantially reduced. The dilution during titration can be kept low by using a concentrated solution of titrating agent, but is easily allowed for by multiplying the values of $(T_1^{-1} - T_0^{-1})$ by V/V_0, where V_0 is the initial volume of the solution and V the volume after addition of titrating agent.

Other applications of the titration technique, for example, to the study of relative stability constants of different complexes in solution, readily suggest themselves.

It is hoped to publish more detailed accounts of the technique and experimental results elsewhere.

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A Dose Test for Irradiated Polyethylene

Although a large body of results has been published on the changes of physical properties induced in ethylene polymers by irradiation, no description of an actual dose test has come to our notice. It happens during electron irradiation of objects that such factors as thickness may influence the dose received at any point so that it is desirable to have available a test which can be used to assess

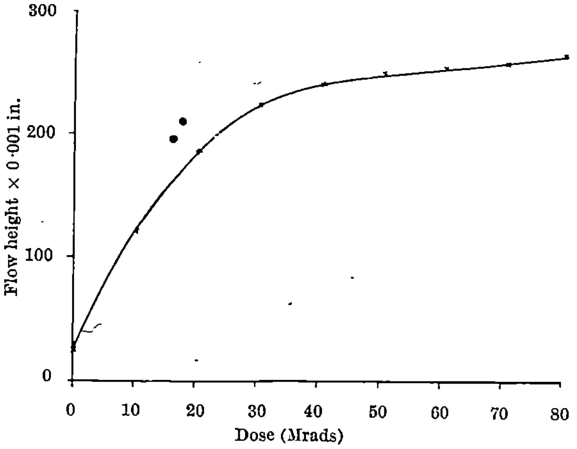

Fig. 1

the radiation dose received by a small amount of material.

In the case of polyethylene, Charlesby and Hancock[1] studied the effect of radiation dose on the relationship between elastic modulus and temperature. From this work a dose-evaluation test could easily be developed, but rather large test samples are required. Other work, which was the starting point for the present study, is due to Ballentine *et al.*[2] and to Lanza[3], who have shown that polyethylene acquires a progressive resistance to deformation with increasing radiation dose, and that the effect shows better at higher test temperatures. Their work does not go far enough for an accurate dose test to be derived from their results.

We have studied the deformation of irradiated polyethylene test pieces using a Williams plastimeter. Under a loading of 5 kgm. on a standard test piece at 150° C. the deformation in 3 min. varies with dose received up to 80 Mrad (Fig. 1). These particular data refer to 'Alkathene 2' (Imperial Chemical Industries, Ltd.) but similar results are obtained with other polyethylenes. The test can only be applied to samples from which cylindrical test pieces may be machined, or to sheets from which disks may be punched to make such a test piece; moulded test pieces at 150° C. revert to their original shape before moulding, so giving irregular cylinders. This effect is due to the well-known 'elastic memory'.

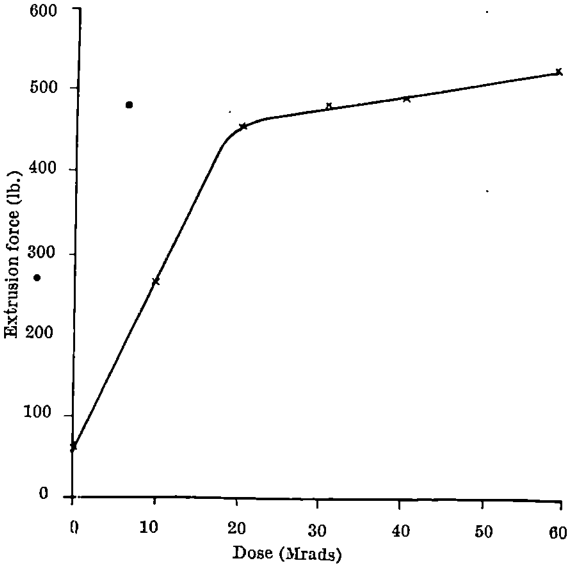

Fig. 2

To overcome this limitation another test has been developed in which the polyethylene is extruded at 150° C. using a Hounsfield tensometer with extrusion attachment. After a few moments the extrusion pressure settles down to a steady value which depends upon the dose received by the polyethylene (Fig. 2). These results refer to 'Alkathene 2' and also to highly expanded cellular polyethylene, which cannot be tested by the Williams plastimeter method.

The methods given appear to be suitable for testing all types of polyethylene for dose received where weights of only a few grams are available.

We are grateful to Mr. W. E. Simpson for helpful discussion and to Mr. T. R. Scott, director of research, for permission to publish this communication.

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Secondary Ionization in Humid Air

Recent measurements of Townsend ionization coefficients by Prasad and Craggs[1] in these laboratories have revealed large variations in the values obtained for the secondary ionization coefficient γ in discharge gaps in air containing water vapour. For example, in humid air at a total pressure of 150 mm. mercury with a partial pressure of 15 mm. mercury of water vapour, its value for a 'Dural' cathode is $7 \cdot 5 \times 10^{-8}$ at $E/p = 45$ V./cm./mm. mercury as compared with a value of $2 \cdot 3 \times 10^{-5}$ in dry air at the same total pressure and electric field.

On the assumption that the secondary ionization mechanism is attributable to photoelectric action at the cathode, as is generally considered to be the case in air at low values of E/p, then it is possible that the observed large reduction in the secondary ionization coefficient may be caused by the absorption of photons by the water vapour present. Its value may then be expected to vary approximately according to the relation:

$$\gamma = \gamma_0 \exp(-\mu p_w d)$$

where γ_0 is the value of γ at $p_w = 0$, p_w is the partial pressure of water vapour in millimetres of mercury, μ is the absorption coefficient at $p_w = 1$ mm. mercury and d is the gap-length in cm.

In order to check whether this relation holds in the case of humid air, the values of $\ln\gamma$ have been plotted as a function of $p_w d$, as shown in Fig. 1. The circled points denote the values of $\ln\gamma$ at different partial pressures of water vapour, up to 15 mm. mercury, in air at a total pressure of 150 mm. mercury. The crossed points denote the values at several gap-lengths, ranging from 1·3 to 4·2 cm., in air at a total pressure of 150 mm. mercury containing 9 mm. mercury pressure of water vapour. Both sets of points are roughly collinear, as is to be expected if photoabsorption is affecting the secondary emission from the cathode. The approximate value of the absorption coefficient, as determined by the slope of the line through the points, is $\mu \sim 0 \cdot 2$ cm.$^{-1}$ at $p_w = 1$ mm. mercury.

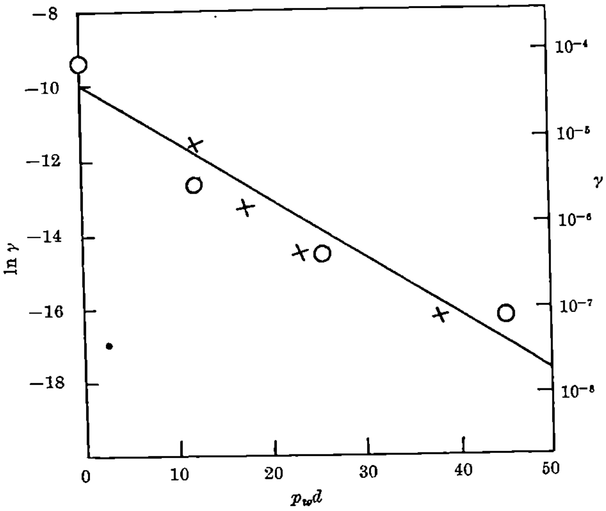

Fig. 1

Usually variations of the secondary ionization coefficient in Townsend discharge studies have been explained by consideration of changes in cathode work function, possibly caused by oxide layers or by adsorption of oxygen and other gases on the cathode surface. There is no doubt that surface conditions greatly affect it, and it is possible that in humid air a layer of water on the cathode surface could be responsible for the large fall in secondary emission. But the observation that the coefficient varies roughly exponentially with $p_w d$ suggests strongly that photoabsorption may also be an important factor in determining its value in humid air. This would not be inconsistent with other evidence as, for example, in Geiger counters, where absorption in methane has been found to reduce secondary photoelectric emission from cathodes. According to Weissler[2], absorption in methane does not occur at wave-lengths greater than about 1400 A., whereas in water vapour absorption is observed at wave-lengths up to about 1900 A. Raether[3] has also reported greatly reduced values of the secondary ionization coefficient in gases containing methane or alcohol.

Even in the absence of water vapour, it is possible that photoabsorption may affect the values of the coefficient of secondary ionization. The results for dry air show a steady fall in γ with decreasing value of the product of gas pressure p and the breakdown gap-length d. When the values of lnγ are plotted as a function of pd, over the range 100–600 mm. mercury × cm., a roughly linear relation is obtained with a slope giving $\mu \sim 8 \times 10^{-3}$ cm.$^{-1}$ at $p = 1$ mm. mercury. The result is complicated by the fact that the magnitude of E/p at breakdown increases with decreasing values of pd. Nevertheless, the suggestion that absorption may affect the coefficient of secondary ionization even in dry air does not appear unreasonable if one notes that, according to Weissler[2], absorption occurs in oxygen at wave-lengths up to about 1700 A.

The above preliminary views are put forward tentatively as a possible explanation of the variations observed by Prasad and Craggs in their measurements of the secondary ionization coefficient. As their experiments were not designed to examine directly the effect of absorption on the secondary ionization coefficient, the deductions that can be made based on their results are limited. There does appear to be sufficient evidence, however, to indicate that absorption may be an important factor in determining its value in air at higher pressures, particularly in the presence of water vapour, and further specially designed experiments are required to investigate the effect.

If the value of the secondary ionization coefficient does in fact fall to a value less than about exp(−18), that is, $\gamma < 10^{-8}$ approximately, the point arises as to whether the Townsend mechanism will still determine the onset of a spark at the minimum breakdown potential. For the multiplication in an avalanche will then be sufficient, greater than about exp(18), to produce a space-charge field of the order required to cause the transition from a single avalanche to a streamer, as observed in cloud-chamber experiments.

I acknowledge the permission of Prasad and Craggs to refer to their results before publication, and also the support given to this work by the Electrical Research Association, at the request of which the studies of ionization in humid air have been made.

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RADIOBIOLOGY

Uptake of Strontium by Pasture Plants and its Possible Significance in Relation to the Fall-out of Strontium-90

Vose and Koontz[1] have lately compared the absorption of strontium-90 and calcium by six species of clover and six species of grass grown in pots containing three contrasting soil types. Their results support the conclusion, previously advanced on less complete results[2], that plant species differ little in the manner in which they distinguish between strontium-90 and calcium. It is well known that the calcium content of clovers is usually higher than that of grasses. Thus, as Vose and Koontz have noted, the absorption of strontium-90 from uniformly contaminated soil will lead to higher concentrations of strontium-90 per unit weight of tissue in clovers than in grasses.

While there can be no disagreement with the results of Vose and Koontz, their conclusion, "It is apparent that if the strontium-90 level in milk should ever rise to a level which, maintained over a period of time, might give cause for concern, it would be desirable to restrict dairy cows to an all-grass diet", appears open to question since :

(1) It is well established that when cattle are fed on a normal diet the ratio of strontium-90 to calcium in their milk depends primarily on the ratio of strontium-90 to calcium in their total diet, being approximately one-seventh of that quantity[3]. Vose and Koontz have shown that the ratios of strontium-90 to calcium in grass and clover grown on uniformly contaminated soil are similar; thus there are no grounds for postulating that the contamination of milk will change when freely grazing cattle are supplied with clover as opposed to grass.

(2) The view that the present levels of strontium-90 from world-wide fall-out in milk are due primarily to it lodging directly on the aerial tissues of plants

and not entering the soil[3] has lately received strong support from the observation of high ratios of strontium-89 to strontium-90 in milk[4,5]. There is no evidence that the aerial entrapment of strontium-90 by clovers exceeds that by grasses; thus the higher calcium content of clovers could lead to a lower ratio of strontium-90 to calcium in clovers than in grasses when aerial contamination is important.

(3) In so far as the contamination of pasture species with fall-out is due to absorption from soil, it is most important to consider the depth from which plant roots absorb their nutrients; a particular reason for so doing is the fact that the major part of the strontium-90 which enters undisturbed soil from fall-out is retained in the upper 5 cm. of soil[6]. Pasture grasses are relatively shallow-rooted while the root-systems of some legumes, notably lucerne, extend to considerably greater depths. Experimental results accord with the view that in these circumstances the ratio of strontium-90 to calcium is least in the more deeply rooted species[7]. For this reason experiments in pot culture, such as Vose and Koontz have described, do not necessarily indicate the situation which will occur under field conditions.

Thus, whereas when plants absorb strontium-90 from uniformly contaminated soil the balance between grass and clover in pastures appears unlikely to be an important factor in determining the strontium-90 content of milk, the presence of clovers in pasture may, under other circumstances, reduce, rather than enhance, the strontium-90 content of milk.

No final statement can yet be made on many aspects of this subject, which is under intensive examination in a number of laboratories; at present, however, there appear to be no valid grounds for suspecting that the presence of clovers in contaminated pastures is likely to increase the radiation dose to the population.

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Separation of Strontium-90 from Calcium in Milk

Attention has recently been directed to the use of ion-exchange methods for alkaline earth separations and to the application of these techniques in the determination of radiostrontium in biological materials[1,4]. The measurement of environmental levels of radionuclides often necessitates the use of comparatively large samples of biological material and involves, in the case of liquid milk, a tedious evaporation procedure[2]. In an attempt to meet the need for a more convenient approach, a study was made of the extent of exchange, on cationic resin columns, of calcium and strontium absorbed from milk passed directly on to the columns.

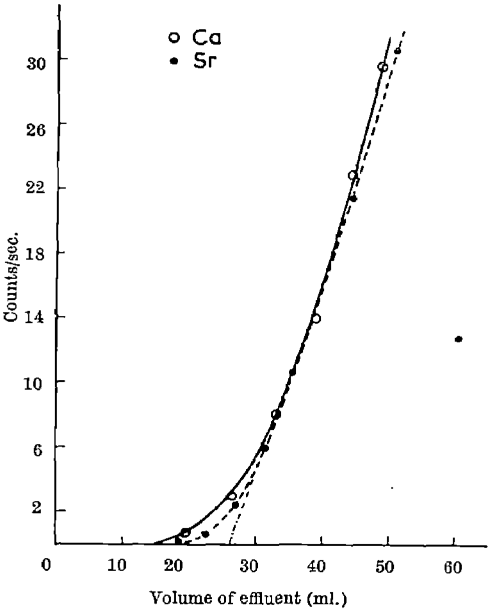

Fig. 1. Calcium, ○, and strontium, ●, breakthrough. Flow-rate, 0·14 ml./cm.^{2}/min.; temperature, 22° C.; column-length, 7·5 cm.

Whole milk samples, in which the natural calcium and strontium were 'spiked' with calcium-45 (0·25 MeV.β) and strontium-85 (0·51 MeV.γ), were run on to columns of a cationic exchange resin ('Zeo Karb' 225, 50–100 mesh, sodium form) and measurements were made of the β- and γ-activities in known volumes of the effluent. The breakthrough capacity for calcium, as indicated by a significant rise in counting rate (Fig. 1), corresponded to the value expected on the basis of capacity determinations carried out by potentiometric titration with sodium hydroxide. Since the ratio of calcium to total strontium (that is, natural strontium and strontium-85) in the milk is high, the resin capacity will be measured primarily by the retention of the calcium component. The observed equality of capacity for the two ions indicates removal of strontium by the large excess of calcium. For volumes of milk containing insufficient calcium to produce resin saturation, gravimetric analysis on influent and effluent solutions showed a quantitative retention of calcium (experimental error ±1 per cent). From parallel estimations of the casein content[3] it was concluded that there was zero retention of casein (experimental error ±2 per cent) indicative of complete breakdown of the calcium–casein complex.

Investigation of the elution characteristics for absorbed calcium and strontium was made using ethylenediamine tetraacetic acid as elutriant. Variations in the eluate of the specific activity of calcium-45 and strontium-85 added to the milk were observed in small-volume fractions collected at defined intervals, and also by continuous monitoring of the eluate passing through a flow counter (20th Century Electronics). The results, illustrated in Fig. 2, for elution at *p*H 8 showed good recovery (>90 per cent) of both calcium and strontium fractions. Further tests, using a range of different *p*H values for the elutriant, gave results in keeping with those described by Davis[1]. No interference with

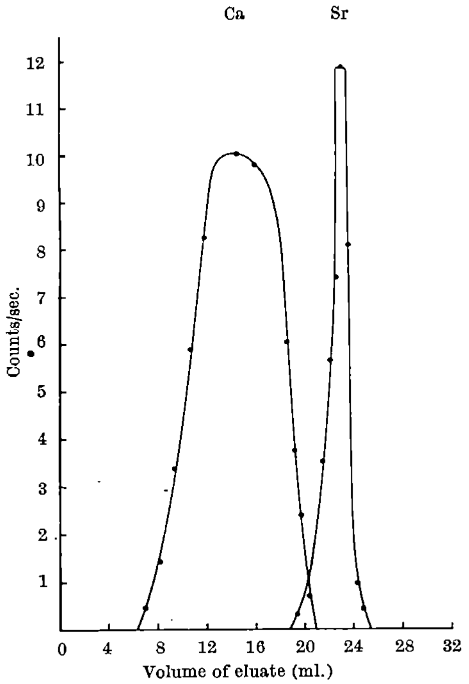

Fig. 2. Separation of calcium and strontium from 1 ml. of milk. Eluting solution : 1 per cent tetra sodium salt of ethylene diamine tetraacetic acid. *p*H 8. Flow-rate, 0·17 ml./cm.²/min. ; column-length, 16·5 cm. ; temperature, 22° C.

column operation was experienced from the milk-fat component, and the resin was readily regenerated for further use. These techniques may therefore be applied satisfactorily to the separation of calcium-free strontium in high yield directly from liquid milk.

I am indebted to Prof. W. V. Mayneord in whose Department the above work was carried out, and to the Medical Research Council for financial aid.

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BIOCHEMISTRY

Position of the Fatty Acids in Cardiolipin

Evidence was obtained previously[1-3] that cardiolipin is composed of two phosphoric acid, three glycerol and four fatty acid residues. According to this structure the polyglycerophosphate skeleton (1) has five hydroxyl groups available for esterification.

$$CH_2OH.CHOH.CH_2O.P : O(OH).CH_2O.CHOH.CH_2O.P : O(OH).CH_2O.CHOH.CH_2OH \quad (1)$$

The position of the fatty acids has now been ascertained by identification of the fragments obtained on hydrolysis of cardiolipin in conditions in which splitting of the phosphoric diester bonds take place preferentially with little rupture of the fatty acid ester bonds.

Cardiolipin (620 μmoles phosphorus), prepared from ox heart muscle by the method of Faure and Morelec-Coulon[4], was heated 90 min. in 50 ml. 90 per cent (v/v) acetic acid at 100° C., and after removal of the acetic acid *in vacuo* the water-soluble and ether-soluble fractions were separated. The ether-soluble fraction contained 68 per cent of the total glycerol, 19 per cent of the phosphorus and 98 per cent of the total fatty acids, only 5 per cent of which were free. By chromatography on silicic acid according to Borgström[5] 76 per cent of the fatty acids were recovered in the diglyceride fraction (485 μmoles ; molar ratio fatty acid–fatty acid ester–glycerol–phosphorus, 1·92 : 1·96 : 1·0 : 0 ; 1·7 double bonds/mole fatty acid) ; by periodic acid oxidation, not more than 2 per cent of this fraction was present as monoglyceride. The remaining fatty acids and the ether-soluble phosphorus were recovered in phosphatide fractions in partly degraded forms (phosphorus–glycerol–fatty acid, 1 : 1·1 : 2·2).

The water-soluble fraction of the hydrolysate contained 80 per cent (500 μmoles) of the phosphorus and 32 per cent (295 μmoles) of the glycerol, combined in a form hydrolysable by phosphomonoesterase ; not more than 10 per cent of the phosphorus, however, was present as glycerolmonophosphate, as estimated by Burmaster's method[6], and no free glycerol was detected. On fractionation 80 per cent of the water-soluble phosphorus was recovered as a barium salt sparingly soluble in water, corresponding in composition to barium glyceroldiphosphate (phosphorus–glycerol–barium, 2·0 : 1·06 : 2·2).

The main products of hydrolysis were therefore glyceroldiphosphate and diglycerides in molar proportion 1 : 2. These results are incompatible with the structure proposed for cardiolipin by Pangborn[7] (a chain of four glycerol and three phosphoric acid residues, in which all six available hydroxyl groups are acylated), which entails the formation on hydrolysis of free fatty acid in proportion to the water-soluble phosphoric ester formed. The results are consistent with a structure for cardiolipin as a derivative of 1, in which the terminal glycerol residues are esterified as diglycerides, leaving a free hydroxyl group on the middle glycerol residue.

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Differential Response of Human Serum Cholinesterase Types to an Inhibitor in Potato

Differences in the degree of inhibition of the activity of human serum cholinesterase (pseudocholinesterase) produced *in vitro* by the local anæsthetic dibucaine (nupercaine) make it possible to classify individuals into three distinct types according to the character of the cholinesterase present in their serum[1]. These types are inherited, and are thought to be determined by a pair of allelic genes each of which is responsible for the synthesis of a distinct form of

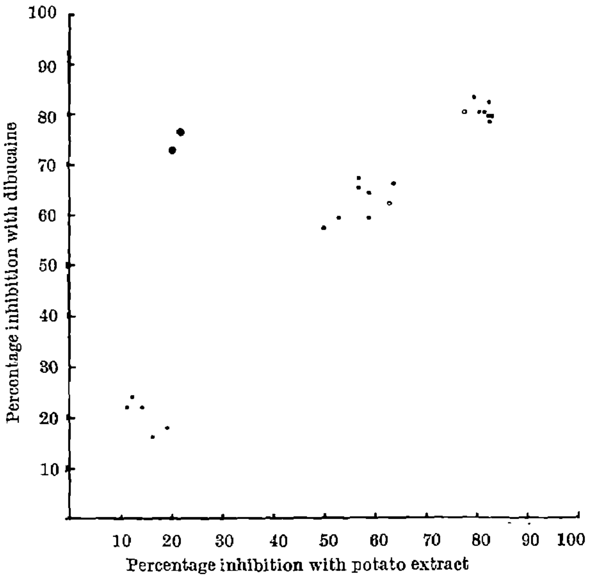

Fig. 1. Relation between percentage inhibition with dibucaine and with a potato-peel extract of pseudocholinesterase in plasmas from 21 different individuals

serum cholinesterase[2]. The two types of homozygotes each have only one of these esterases in their serum, while the heterozygote is believed to have both of them in about equal amounts[3]. The classification of the three phenotypes may be achieved by a number of cholinesterase inhibitors besides dibucaine[3]. However, there also exist certain cholinesterase inhibitors, such as tetraethylpyrophosphonate and di*iso*propylfluorophosphonate which fail to discriminate between the three types, presumably because their mode of action is different[3].

Orgell, Vaidya, and Dahm[4] have recently demonstrated that aqueous extracts of a number of solanaceous plants are capable of inhibiting human serum cholinesterase. It was of interest to see whether or not this common naturally occurring inhibitor acted differently on the three genetically determined phenotypes. A convenient source of this inhibitor is potato, and in the present experiments extracts of potato peel were used because it had been shown that the concentration of the inhibitor was considerably greater in the peel than in the inner part of the tuber.

A series of plasmas from individuals of the three cholinesterase phenotypes were used as a source of the enzymes. They had been typed according to the method of Kalow and Genest[1], using a 1-in-100 dilution of plasma, with 5×10^{-5} *M* benzoylcholine as substrate, 10^{-5} *M* dibucaine as inhibitor, in *M*/15 phosphate buffer *p*H 7·4. The reactions were followed spectrophotometrically at 240 mμ. The percentage inhibition obtained under these conditions was 77–83 per cent for the so-called 'usual' phenotype, 53–67 for the 'intermediate' phenotype, and 16–24 for the 'atypical' phenotype. The plasmas of the uncommon 'atypical' phenotype were mainly obtained from individuals who had been found to be unusually sensitive to the muscle relaxant succinylcholine when this was administered during anæsthesia. The individuals of the 'intermediate' phenotype were identified either in the course of studies of the families of the 'atypical' individuals or during random population surveys, where they constitute about 3 or 4 per cent of all people tested.

In the experiments with the potato extract the same procedure was adopted as mentioned above except that the extract was used as inhibitor in place of the dibucaine. The extract was prepared by macerating 85 gm. of potato peel in 300 ml. of water, and then filtering through gauze. A 1-in-100 dilution of the filtrate in *M*/15 phosphate buffer *p*H 7·4 was used as the inhibitor.

Results from a typical experiment using sera of 8 individuals with the 'usual' phenotype, 8 with the 'intermediate' phenotype, and 5 with the 'atypical' phenotype, are shown in Fig. 1. It is apparent that the potato inhibitor discriminates between the three groups just as sharply as does dibucaine, and there is a good correlation between the two sets of inhibition values. Several different batches of potatoes were tested with the same kind of results. Although the concentration of the inhibitor appears to vary slightly from batch to batch, clear discrimination of the three types was obtained in each case using a 1-in-100 dilution of the extract prepared as above.

The nature of the serum cholinesterase inhibitor in potato is not yet known. However, the occurrence in a common foodstuff of a substance which behaves differentially with the three serum cholinesterase phenotypes raises the question as to whether it may not be connected in some way with the genetical polymorphism determining the occurrence of alternative forms of serum cholinesterase in human populations.

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An Alteration in the Excretion of Free Serine in Urine from Irradiated Humans

A number of investigators have been interested in the urinary excretion of amino-acids following total-body irradiation[1]. No one has used the quantitative column procedure of Moore, Spackman and Stein[2]. This preliminary communication is based on their procedure.

In June 1958 eight workmen were accidentally exposed to total-body gamma and neutron irradiation at one of the U.S. Atomic Energy Commission's installations in Oak Ridge. These men were studied at the Medical Division of the Oak Ridge Institute of Nuclear Studies. During the first 16 days the clinical manifestations of irradiation were minor, and the patients were ambulatory and ate well. There was a slight gain in weight during this period.

Urine was refrigerated (about 5° C.) after it was voided and, when a 24-hr. collection was complete, the volume was measured and aliquots for various procedures taken. As soon as the measurement and sampling was complete, all specimens were stored in the deep-freeze about (−15° C.) until they were analysed. Aliquots (2 ml.) of filtered urine were analysed without desalting. A commercial model of the automatic apparatus of Spackman, Stein and Moore[3] was used. Other analyses and analyses of hydrolysed urine[4] were done with the fraction-collector method[2].

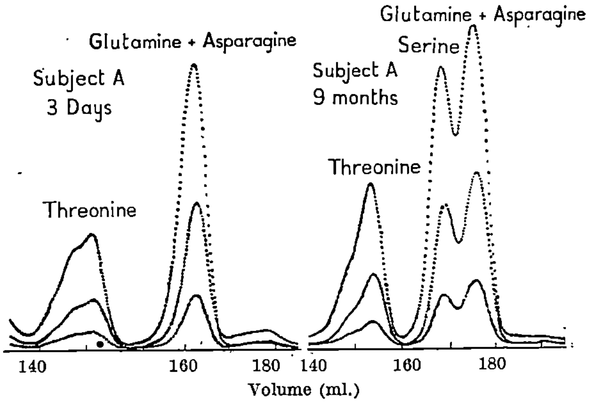

Fig. 1. Part of a recorder tracing of ninhydrin amino-acid colour taken from analyses of urinary amino-acids excreted by a man who was accidentally exposed to 365 rad of whole-body gamma and neutron irradiation. Serine is absent from the urine excreted 3 days after exposure

Among the most interesting results is the decrease in urinary excretion of free serine. This decrease is illustrated in Fig. 1. An analysis of a sample of urine excreted nearly nine months after the accident that shows the presence of free serine is included for comparison. Free serine was decreased even on the first day after irradiation and was apparently absent from this patient's urine three days after exposure. Traces only were excreted on the second and tenth days after irradiation. On the fourth and sixteenth days no serine was excreted. Serine was present in the urine after acid hydrolysis.

Serine was decreased but not absent from urine excreted by a child with leukæmia during the second day after 800 r. total-body irradiation. This irradiation was from a cobalt-60 source and, therefore, pure gamma. In contrast, there was a considerable neutron component in the accidental irradiation.

We do not have analyses of plasma and, therefore, do not know whether the reduced serine excretion is a renal effect or whether there is a change in the intermediary metabolism of this amino-acid in irradiated humans.

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* Under contract with the United States Atomic Energy Commission.

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Mucoprotein of Bronchial Mucus Gel

In the absence of acute infection, the excessive bronchial secretion in chronic bronchitis is mucoid and owes its viscidity to a gel structure. This is apparent as an oriented fibrous network in the polarizing and electron microscopes[1-3], and there is a yield-value for disruption of the gel[2-4]. Mucoprotein can be isolated in yields of about 60 per cent of the total nitrogen by the procedure of Curtain and Pye[5], and has the composition shown in Table 1. Mannose and galactose are also constant constituents[1-3].

Table 1. The Composition of Bronchial Mucoprotein, as Percentage of Dry Weight

Constituent	Gm. percentage of dry-weight $M \pm S.D.$ (13 samples)
Nitrogen	8·6 ± 1·1
Total reducing sugar, expressed as glucose	19·5 ± 4·9
Hexosamine	6·1 ± 1·7
Fucose	5·1 ± 1·3
Sialic acid	4·2 ± 1·3
Bound sulphate as sulphur	0·0 – 0·2
Total phosphorus	*c.* 0·25

The viscous solutions are opalescent and gelatinous at concentrations above 1–2 per cent. The ultraviolet absorption in water or 0·1 *N* hydrochloric acid, due to aromatic amino-acids, has a maximum at 270–275 mμ (ε(N) about 190), with less scatter in 0·1 *N* sodium hydroxide and 280–284 mμ maximum (ε(N) about 110). On paper electrophoresis at *p*H 8·6 most of the material moves towards the anode as a peak giving reactions for protein and polysaccharide; but small fractions run in advance and remain at the origin. Boundary-electrophoretic results are comparable; there is no gross heterogeneity and less negative charge at *p*H 4·5 than at 8·5. The composition and properties are similar to those found by Brogan[6] for mucoprotein in the insoluble fraction after acid-peptic digestion of acetone-dried sputum.

In Ostwald viscometers there is an exponential relationship of relative viscosity to concentration up to 1 per cent (w/v). Although this is similar to deoxyribonucleic acid, there is no evidence for more than traces of this substance in the mucoprotein, and deoxyribonuclease does not affect the viscosity in the presence of magnesium ions. The intrinsic (limiting) viscosity of the mucoprotein has been determined for dilute, salt-free solutions (0·001–0·025 gm. protein/100 ml.), using Ostwald viscometers B.S. 1 and 2 at 25° C., and applying a kinetic energy correction to No. 2. Non-Newtonian at higher concentrations, solutions of mucoprotein below 0·02 gm. protein/100 ml. give comparable viscosities at different rates of shear. Plotting the reduced specific viscosity (η_{sp}/c) against concentration (c) and extrapolating fitted lines to zero concentration, the values for intrinsic viscosity are 8·1 (± 0·07) from viscometer 1, 8·8 (± 0·57) from viscometer 2, and do not differ within the limits of the sampling errors[7]. The partial specific volume is 0·69 by pycnometry. This gives an average viscosity increment of 1225, corresponding to an axial ratio[8] of about 150. Although this has little precision, since hydration is unknown, orientation of flow is likely to have occurred, and the electron-microscope suggests flexible chains and a greatly elongated molecule is indicated. Similar results were obtained by Curtain[9] for urinary mucoprotein.

Physical differences exist between bronchial and urinary mucoproteins. Curtain[9] found that solutions of the latter increase in viscosity with increasing ionic strength; precipitation is maximal in 0·58 *M* sodium chloride[6,10]. Very low concentrations of ions lower the viscosity of bronchial mucoprotein; with sodium chloride, viscosity is minimal at 0·04 *M*, increasing very slightly up to 4 *M*, without precipitation. The behaviour on centrifugation suggests modification of a gel structure. The aqueous 'solutions' are stable on standing at 5° C. (though occasionally an insoluble syneresed coagulum separates), but a loose gelatinous deposit forms with quite low centrifugal force (about 60 per cent of the protein

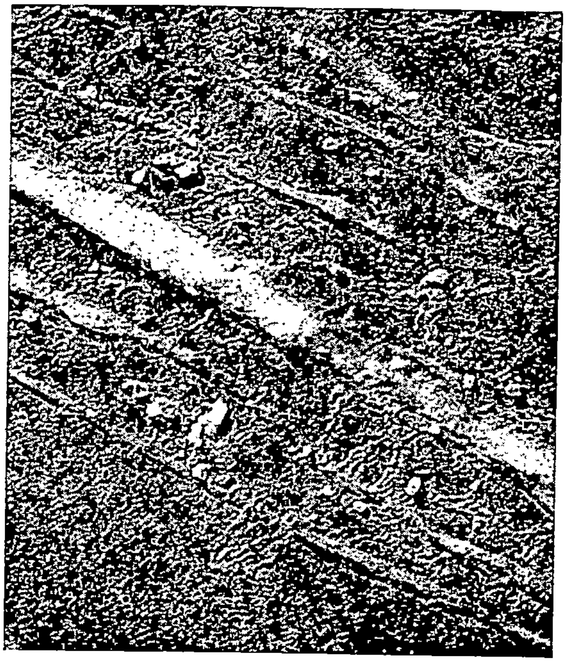

Fig. 1. Electron-micrograph of bronchial mucoprotein, shadowed with gold–palladium. (× 22,500)

at 9,000 r.p.m. for 1 hr.); in 0·15 *M* sodium chloride, more than 75 per cent of protein deposits in compact form. These deposits redisperse readily. Agents which modify hydrogen-bonding cause a fall in viscosity comparable to dilute salts, but very little deposits on centrifugation; for example, 6 *M* urea, 3·2 *M* guanidine hydrochloride, and particularly 8 *M* lithium bromide. In the ultra-centrifuge at speeds between 4 and 50 × 10^3 r.p.m., and at protein concentrations of 0·2 and 0·02 gm./100 ml. of 0·04 *M* sodium chloride, the concentration of the bulk of the solution diminishes rapidly, but with little movement of the peak. Gel deformation in the centrifugal field may well account for this. Tamm, Bugher and Horsfall[11] obtained $S_{20} = 29 \cdot 5$ for urinary mucoprotein and molecular weight $7 = 10^6$; however, there is likely to be a range of molecular size in this material also[10].

The bronchial mucoprotein forms oriented inclusions in crystals of sodium chloride[1,12]. By electron microscopy, the fibrils range in diameter from 0·1–0·2μ to 400 A. Between these, smaller, flexible micro-fibrils are seen (Fig. 1), and measurement of gold–palladium-shadowed preparations indicates that these are ribbon-like with mean cross-sectional dimensions, 304 A. wide by 74 A. thick, but occasionally about half this size. Although certainly composed of several molecular units, these approach the fundamental dimensions for a number of stable fibriform bodies[13]. A beaded appearance in the smaller micro-fibrils possibly indicates sub-units. There are similarities between the micro-fibrils and those of the urinary mucoprotein of Porter and Tamm[14].

In conclusion, it seems that the gel-structure of bronchial mucus is still present in the mucoprotein 'solutions' derived from it.

Note added in proof: Recent electron-microscopic evidence indicates breakdown of the gel-structure into short, rigid sub-units in 8 *M* lithium bromide.

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Phosvitin in the Serum of the Hen

A PHOSPHOPROTEIN fraction appears in the serum of the hen in association with the onset of laying[1,2] or in the serum of the immature bird on treatment with œstrogen[3]. It can be shown by zone electrophoresis on filter paper that two new major protein fractions appear in the serum on œstrogenization, one of these being specially rich in protein phosphorus[4]. The demonstration by Mecham and Olcott[5] of the existence of phosvitin in egg-yolk, and the view that yolk constituents are synthesized in the liver and transferred thence to the ovary in the blood plasma, prompted us to examine the blood of the hen for presence of phosvitin.

Four laying hens were each given 2 mgm. œstradiol benzoate per day for 5 days. The birds were then bled and 200 ml. serum was recovered. Crude lipovitellin complex was precipitated by bringing the serum to *p*H 5·3 and then adding an equal volume of distilled water. The precipitate was separated on the centrifuge, re-dissolved in 1 per cent sodium chloride and re-precipitated by ten-fold dilution with distilled water. The precipitate was worked up for phosvitin by the method of Joubert and Cook[6] as though it were egg-yolk, with the exception that an international refrigerated centrifuge Model *PR*1 was used instead of a high-speed centrifuge as used by Joubert and Cook. The method of Joubert and Cook avoids complications introduced by ether extraction.

After the final dialysis, the water-clear supernatant yielded, on freeze-drying, 150 mgm. of a white protein that contained 10·1 per cent phosphorus and 12·3 per cent nitrogen. The protein behaved as a single component and displayed the same mobility on paper electropherograms as did samples of phosvitin prepared from egg-yolk by the same technique, and gave no lipid stain.

We believe that this result represents the first occasion on which phosvitin has been identified as a constituent of the hen's blood. We consider further that the slow-moving 'PP' lipoprotein fraction, rich in protein phosphorus, on electropherograms of sera of œstrogenized and laying birds[4] probably represents a lipovitellin–phosvitin–γ-livetin complex in the sense in which this term is used by Joubert and Cook[6]. The 'PP' fraction was originally distinguished by the use of methanolic veronal buffer, but more recently we have been able to distinguish it by zone electrophoresis in aqueous buffer (*p*H 8·6, μ 0·05). The second, somewhat more mobile, lipoprotein fraction ("fraction 8" of Vanstone *et al.*[7]) presumably corresponds mainly to lipovitellenin.

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Basic Substances as Synergists for Fat Antioxidants

ADDED fatty acids decrease the effectiveness of a number of antioxidants in marine and other oils and fats[1]. It has now been demonstrated that many oil-soluble basic substances may act as synergists. For example, a primary amine (octadecylamine, ODA), a secondary amine (proline), and a tertiary amine (tri*iso*octylamine, TOA) provided unexpectedly great protection against oxidation to oils containing added 6-ethoxy-2,2,4-trimethyl-1,2-dihydroquinoline (EMQ, 'Santoquin'), whereas in the absence of the last-named they conferred only slight or no protection at the same levels (Table 1).

The effects of the various basic additives differed with each antioxidant. For example, in general they were synergists to 2-tertiarybutyl-4-methoxyphenol (BHA) but had no effect or acted as antagonists to 2,6-ditertiarybutyl-4-methoxyphenol (BHT). They were also more effective with γ-tocopherol than with α-tocopherol. In this respect they have been found useful in differentiating the various tocopherols with regard to antioxidant effectiveness.

Substrates also modified the respective activities. With the samples of highly purified trilinolein available to us (Hormel Foundation), octadecylamine acted as an antagonist to α-tocopherol and synergist to γ-tocopherol, whereas in menhaden oil octadecylamine was synergistic with both.

Proline was particularly effective in vegetable oils, probably acting in conjunction with the natural antioxidants. For example, samples of a refined olive oil containing 0, 0·025 and 0·05 per cent added proline had induction periods at 60° C. of 4, 12 and 23 days, respectively.

The synergistic effects of phospholipids and of some amino-acids on phenolic type antioxidants have been recognized for a number of years[2]. It appears likely that these effects may be mediated through the basic groups of such compounds, modified by solubility, heavy-metal chelating, and other properties. With respect to phospholipids, this contrasts with a previous suggestion[3] that the phosphate portion of the molecule was primarily involved.

Table 1. EFFECT OF MIXTURES OF ANTIOXIDANTS WITH BASIC SYNERGISTS ON MENHADEN OIL AND TRILINOLEIN

Antioxidant	Basic additive	Induction period*–Days (50° C.)	
		Menhaden oil†	Trilinolein
EMQ	None	3	31
,,	ODA	28	56
,,	Proline	87	61
,,	TOA	104	41
,,	Phospholipid‡	33	—
BHA§	None	2	12
,,	TOA	11	15
BHT	None	4	19
,,	TOA	2	12
α-Tocopherol	None	2	10
,,	ODA	3	6
,,	Proline	3	18
,,	TOA	17	7
γ-Tocopherol	None	3	13
,,	ODA	9	31
,,	Proline	25	—
,,	TOA	36	36
None	None	1	1
,,	ODA	1	1
,,	Proline	1	1
,,	TOA	1	1

* Induction periods were determined by the gain in weight method recently described (ref. 4). 10-ml. beakers containing 200 mgm. substrate plus 0·5 μ*M* of antioxidant and 2·5 μ*M* of basic additive were incubated in a draft oven at 50° C., cooled and weighed once daily (to 0·1 mgm.). The end of the induction period was usually readily detected by a rapid gain in weight and arbitrarily fixed at the time at which the weight gain was 1 mgm.

† The menhaden oil was a commercial alkali-refined product treated to remove peroxides as follows: a 10 per cent solution in light petroleum ether was passed through a column of deactivated alumina and the solvent removed *in vacuo*.

‡ A preparation of yeast lecithin containing 1·89 per cent nitrogen, 4·1 per cent phosphorus, 0·03 per cent amino-nitrogen (D. J. Hanahan).

§ BHA is often designated 2 (or 3)-tertiarybutyl-4-methoxyphenol. The preparation which was used in much of this work contained at least 85 per cent of the 2-tertiarybutyl derivative. Similar results were obtained with the pure 2-isomer.

The progress of this work has been hampered by difficulties in obtaining reproducible runs. The results shown are, however, typical of a number of determinations. Details will be published elsewhere.

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An Improved Method for preparing Pectate Gels

THE routine use of pectate gel media as an aid to the detection of bacteria causing soft rot of plant tissue has been restricted by the difficulty commonly encountered in their preparation. One of the most useful methods is that of Wieringa[1], who adopted the double-layer technique, consisting of a plate of calcium agar over which the pectate solution was poured. Diffusion of calcium ions from the agar brought about the formation of a gel.

In practice it has been found that convenient quantities of liquid pectate solution are difficult to prepare, as a weak gel forms on cooling and during storage. This gel frequently fails to liquefy uniformly on heating, and the resultant lumpy fluid produces unsatisfactory plates. Moreover repeated autoclaving of pectate solutions tends to lower the quality of the final gel.

The addition of disodium salt of ethylenediamine tetraacetic acid in low concentration to the pectate solution prevents the unwanted gel formation. This free-flowing liquid can be autoclaved normally and sterile stocks can be stored indefinitely without losing the ability to form a firm gel in the presence of sufficient calcium ions.

This appears to be due to the activity of the disodium salt as a chelating agent for the calcium ions present in the pectate. The high concentration of these ions diffusing from the calcium agar is sufficient to replace the calcium removed by chelation and, if in excess, to bring about adequate gelling of the pectate.

The procedure which has proved satisfactory in current work on soft rot pseudomonads can be summarized as follows. (*a*) Calcium agar base: peptone (Evans) 0·5, lemco 0·5, calcium lactate 0·5, agar (Davis) 1·5 per cent (sterilize at 15 lb. pressure). (*b*) Pectin solution: mix 2 gm. pectate powder with absolute alcohol to form a thin paste; make up with distilled water to 100 ml. and add 0·1 gm. disodium salt of ethylenediamine tetraacetic acid. Sterilize at 15 lb. pressure. The pectin solution is poured as a thin layer over a plate of the calcium agar (1 cm. deep). The gel sets firmly within 12–24 hr. at 27° C.

The pectate powder used was either 'Sodium polypectate' ('Exchange' brand obtainable from Sunkist Growers (Products, Ltd.), Ontario, California, and S. and S. Services. 72 Victoria Street, Westminster, London, S.W.1) or 'sodium pectate' (A.S.P. Chemical Co., Ltd., Bulstrade, Gerrard's Cross, Bucks).

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Conversion of Caffeic Acid to Esculetin during Paper Chromatography

ESCULETIN was found in an extract of plant tissue which contained caffeic acid. The esculetin was not a natural product but was formed from caffeic acid during the paper-chromatographic purification procedures. This conversion was confirmed by two-dimensional chromatography of authentic caffeic acid.

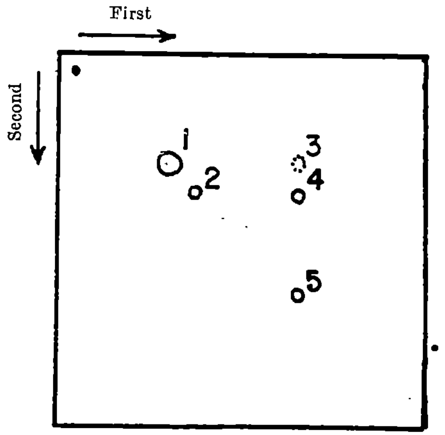
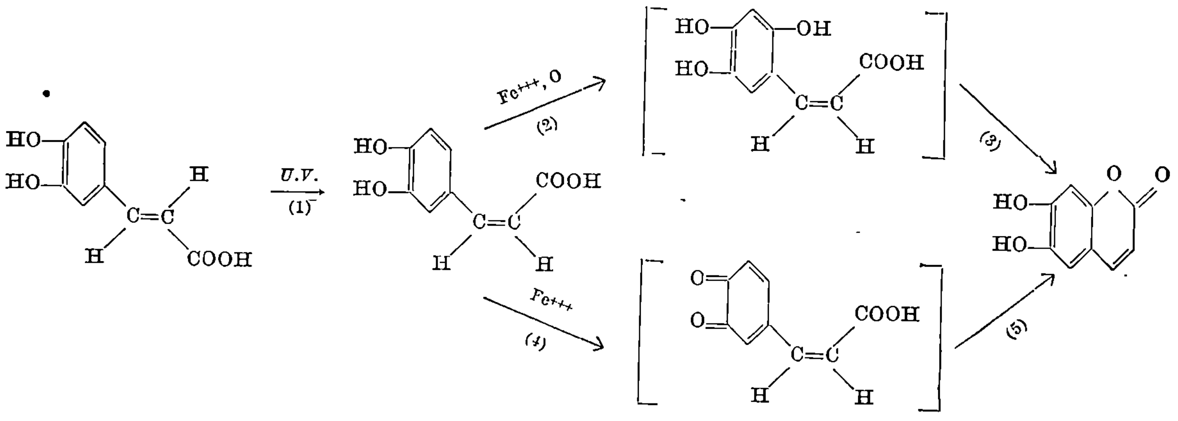


Fig. 1. Chromatogram of caffeic acid. Developing solvent: 5 per cent acetic acid in both dimensions

The fluorescent spots found on a two-dimensional chromatogram of caffeic acid using 5 per cent acetic acid as the solvent in both dimensions are shown in Fig. 1. When the chromatogram is developed in the dark on unwashed or water-washed chromatographic paper, only spot 1 is seen. If the caffeic acid is irradiated with a low intensity ultra-violet lamp for 5 min. at the origin before development, all five of the fluorescent spots are found. If chromatographic paper which has been washed with 0·001 *M* ethylenediamine tetraacetic acid is used, only three of the spots, 1, 3 and 5, are found on the chromatogram of the ultra-violet-irradiated caffeic acid. If the paper washed with ethylenediamine tetraacetic acid is dipped into 0·01 *M* ferric chloride and dried, the developed chromatogram of the ultra-violet-irradiated caffeic acid has all five spots. The spots were identified as: (1) caffeic acid; (2) esculetin; (3) caffeic acid; (4) esculetin; and (5) caffeic acid.

The ultra-violet light converted a part of the *trans*-caffeic acid at the origin to the *cis*-isomer[1]. Chromatography in the first dimension separated the slower moving *trans*-isomer from the faster moving *cis*-isomer. In the second dimension, a small amount of the *cis*-isomer reverted to the *trans*-isomer (spot 3 is quite faint) and esculetin appeared. The formation of the esculetin from the *cis*-caffeic acid is an oxidative reaction requiring metal ions. Esculetin is not found on chromatograms which are developed on ethylenediamine tetraacetic acid washed chromatographic



paper. The conversion of *cis*-caffeic acid to esculetin could proceed through a hydroxylated intermediate or through a quinone. The hydroxylation reaction, step 2, is similar to the hydroxylation of phenols by an ascorbic acid–iron system studied by Undenfriend[2]. The lactone formation, step 3, is analogous to the spontaneous cyclization of *cis*-*o*-coumarin acid to coumarin[1]. An alternative mechanism involves oxidation to the quinone, step 4, with lactone formation by a Michael addition β to the carbonyl followed by aromatization, step 5. This is less likely, however, because Michael additions do not generally occur under mild acid conditions.

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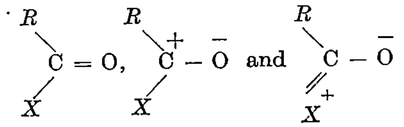
A Proposed Interpretation of Infra-red Spectral Changes occurring upon the Interaction of Polynucleotides

IT has been found that the sodium salts of polyadenylic and polyuridylic acids interact[1–4] with formation of a two-stranded helix[1] with a structure very similar to deoxyribonucleic acid. More recently it was observed that the infra-red spectrum[5] of the mixture of these two acids showed the following marked changes from the summation of the curves of the components: a 39 per cent reduction in intensity of the 1,627 cm.$^{-1}$ band and a 7 cm.$^{-1}$ shift to higher frequency; a decrease in peak height (because of strong overlap the band was not integrated) and an 11 cm.$^{-1}$ shift to higher frequency of the 1,661 cm.$^{-1}$ band. The interaction of the sodium salts of polycytidylic and polyinosinic acids[6] has now been observed in the infra-red[7] with the following result: a marked decrease in intensity of the 1,651 cm.$^{-1}$ peak of the sodium salt of polycytidylic acid (the intensities have not yet been put on a quantitative basis) and a 19 cm.$^{-1}$ shift to higher frequency of the 1,678 cm.$^{-1}$ peak of the sodium salt of polyinosinic acid.

It is possible that an understanding of these changes may be reached by taking into account the change in environment of the vibrating groups after interaction has occurred. A consideration of the helical structure of deoxyribonucleic acid[8,9] and of the polynucleotide pairs[1,6] reveals that the heterocyclic rings are covered on both sides by other such rings at a distance of about 3·4° A. This is no more than a van der Waals separation, and is insufficient to admit water molecules between the planes of the two rings. One result of this helical configuration is, therefore, that the dielectric constant of the immediate environment of the vibrating groups must be considerably diminished, even though water remains in the area which is not between the base pairs.

The purine and pyrimidine bases are hydrogen bonded to water before interaction and to other bases after interaction, but the hydrogen bonds existing after interaction should be stronger than those that existed before[10]. The observed spectral changes, thus, are probably not caused (directly) by the new hydrogen bonds since the usual effect of hydrogen bonding is to decrease frequency and increase intensity rather than the reverse.

The following qualitative considerations, on the other hand, suggest that the observed changes are consistent with a decrease in dielectric constant. The principal resonance forms of the carbonyl group[11] are:



Hydrogen bonding favours the dipolar forms with a resulting shift to lower frequency. A marked decrease in dielectric constant of the medium, however, should diminish the contribution of the forms involving a charge separation and result in a shift to higher frequency. A second result of a decrease in dielectric constant is that there should be a smaller change in dipole moment with the vibration of the bond responsible for the absorption and a consequent reduction in intensity. Experimental results in support of these expectations are cited below.

In studies of frequency and intensity changes in approximately a dozen solvents[12,13] (see also ref. 11), it has been shown that the carbonyl stretching bands show a general trend of increase in frequency and decrease in intensity as the dielectric constant of the medium is decreased. Thus, for example, the frequencies of several ketones increase 11–14 cm.$^{-1}$ on going from chloroform to hexane and 8–9 cm.$^{-1}$ on going from benzene to hexane. There are also 18–36 per cent and 15–20 per cent reductions in intensity for the same solvent changes. *NN*-Diethylacetamide[13] showed a frequency increase of 38 cm.$^{-1}$ for the first solvent change and 15 cm.$^{-1}$ for the second, with intensity reductions of 24 and 20 per cent, respectively. *NN*-Diphenylacetamide showed a similar trend for those solvents in which it was soluble. The directions and approximate magnitudes of these spectral changes are thus consistent with those observed with the polynucleotides. While there are undoubtedly other factors contributing to the observed spectral changes, it is suggested that the above-mentioned decrease in dielectric constant may very well be the most important cause.

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OPHTHALMOLOGY

Regeneration of the Lens of the Eye in the Rabbit

In a recent communication, Chanturishvili[1] reports his re-investigation of the detailed embryology of the lens in Amphibia and refers to work on higher forms in his laboratory at Tiflis. He and his fellow-workers, in particular Sikharulidze[2], are of the opinion that the lens fibres are derived from cells which are neural in origin, and which require for the initiation of fibre production the products of the cytolysis of epidermal elements.

As a corollary of their view of lens development the Tiflis workers have introduced small fragments of cytolysing fœtal tissues into the lens capsules of adult animals from which all easily separable contents had been evacuated. They report that whereas simple evacuation without implant is followed by very little regeneration (the familiar aphakic state following the operation of extracapsular lens extraction), the addition of the implant is followed by the regeneration of a lens nearly normal in size and structure.

On a visit to Tiflis in 1955 one of us (P. G. 'E.) was enabled, by the courtesy of Prof. Chanturishvili, to see something of this work there. Later, Prof. Chanturishvili most kindly placed at our disposal, in the fullest possible detail, particulars of the techniques employed by him and his co-workers.

At Prof. Chanturishvili's suggestion, we repeated here the experimental implantation of cytolysing fœtal tissue taken from the lid commissure of a three-week embryo into the evacuated lens capsules of six normal rabbits according to the technique of Tamara Sikharulidze. We kept suitable control animals in which the lens capsule contents had been simply evacuated without implantation. This work was done because it was hoped that Prof. Chanturishvili would be able to attend the Oxford Ophthalmological Congress and to demonstrate this material of ours there. In the event, he was not able to do so, but these rabbits were demonstrated there by us in July 1958, 12 weeks after operation.

At that time there were marked differences to be seen between those evacuated lenses which had received implants and those which had not. Whereas the animals without implants showed the normal aphakic post-operative condition of collapsed and apposed capsular walls, those which had received implants showed inflated and in some cases spheroidal lens capsules, the contents and shape of which had a refractive power approximating to that of normal lens. This process of regeneration is continuing eleven months after operation.

Prof. Chanturishvili visited this Department in August 1958 and allowed us to examine his embryological preparations and generously presented us with material. He states that about 16 months are needed for full regeneration, but our most promising rabbits have lenses already little different from the normal in size. The iris can be seen to be supported by the convex anterior surface of the lens as in the normal eye, whereas in the aphakic controls the unsupported iris presents a concave surface to the observer.

Assessment of the structural and functional state of each lens in an ophthalmological sense has been made at frequent intervals by evaluation of the refractive condition of each eye as a whole by ophthalmoscopy and skiascopy. Whereas the normal unoperated eye in our rabbits is from zero to two and a half dioptres hypermetropic, the aphakic control eyes have consistently been found to be of the order of ten to fifteen dioptres hypermetropic. By notable contrast, the eyes which had received implants have been found, in the areas of incipient lens regeneration, to be comparable in refractive power to the normal as early as eight weeks after operation.

The progressive variations in shape and appearance of the lens capsule and its contents in each case have also been surveyed by frequent slit-lamp biomicroscopy. In every lens which received a fœtal implant the anterior and posterior capsule walls have become separated in part, and in some instances fully. The lens has assumed a progressively spheroidal shape. Relucence of the substance within the capsule suggests that it possesses optical properties comparable with those of a normal lens and differing from those of aqueous humour.

The approximately lenticular shape of the most successful examples and their relatively transparent and homogeneous contents make possible a satisfactory ophthalmoscopic view of fundus detail. Even in the best, however, there are some variations of optical density still remaining. These may possibly be ascribed to incomplete cytolysis of implanted material, or to incomplete removal of the original contents of the lens capsule. On the other hand, some of them may represent a stage in a process of regeneration not yet complete. Distortions of shape and incomplete separation of the capsule walls, which were found particularly in our first few operations, are probably due to faulty technique.

The preliminary observations reported here seem so far to confirm the findings of the Tiflis workers in the rabbit.

We propose to repeat our work here on a larger scale to allow the sectioning of regenerating lenses at all stages. It seems to us that this filling out of the capsule in so short a time may perhaps be ascribed to the secretion of a 'ground substance', in which fibres may grow later, more probably than to actual immediate growth of functional fibres.

Sikharulidze reports retarded but satisfactory regeneration of lenses in rabbits after the removal of cataracts induced chemically. At present we are engaged in a repetition of our work using rabbits which have received high doses of local irradiation.

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PHYSIOLOGY

Induction of Arginase in Rabbit Epithelium by the Shope Rabbit Papilloma Virus

In studies of the mechanism of action of the Shope virus in causing papillomas on the skin of rabbits, comparative tests were made of active transport of amino-acids into papilloma cells and into normal and hyperplastic rabbit epithelium. The method used was that recently reported by Rogers and Woodhall[1].

Papilloma epithelium taken at intervals varying from 10 days to one month from the time of inoculation of the papilloma virus was cut into tiny pieces, the largest size of which was on the average of 0·25 mm. in diameter, rinsed in Ringer's solution, 50–100 mgm. amounts of tissue added to 1·5 ml. of a synthetic tissue culture media (Media 199, Difco), incubated for 2–20 hr. at 37° C., the cells and cell clumps centrifuged out of the media, the media chromatographed, and the relative amounts of amino-acids remaining determined semi-quantitatively with a Spinco analytrol densitometer. The chromatograms were made using butanol, 40 ; acetic acid, 10 ; water, 50 and aqueous phenol. Normal and hyperplastic skin were entirely similarly treated. The hyperplastic skin was of two sorts ; the 'spontaneous' variety associated with cyclic hair growth and that induced by several treatments of the skin with a 50 : 50 solution of turpentine and acetone. Experiments were done in both Kansas cottontails and domestic rabbits.

A number of differences in the relative amounts of amino-acids removed from the media, as well as differences in which amino-acids were removed, were found. This communication is concerned with only a seemingly qualitative difference relating to arginine uptake. In repeated experiments the papilloma tissue invariably has taken up large amounts of arginine. No demonstrable uptake of arginine has been found in the case of normal or hyperplastic skin. However, as this amino-acid is a common constituent of protein, the uptakes are probably merely too small to measure in this system. Table 1 depicts the results of a typical experiment.

Table 1. ARGININE (PER CENT) REMAINING IN MEDIA AFTER INCUBATION WITH PAPILLOMA OR WITH HYPERPLASTIC SKIN EPITHELIUM

	Period of incubation	
	2 hr.	20 hr.
Papilloma	25	10
Hyperplastic skin	100*	110†

* Equivalent to 0·07 mgm. arginine per c.c.
† Increase from cellular breakdown.

As a result of the above findings, together with the fact that ornithine was regularly found in the media exposed to the papilloma tissue and not at all in the media exposed to skin, it was decided to find whether arginase could be demonstrated in extracts of papilloma tissue and in extracts of normal and hyperplastic skin. The arginase was extracted, concentrated, and tested by standard methods outlined elsewhere[2]. 3 gm. of papilloma tissue were ground to a paste with sand and an extract then made. The concentrated dialysed solution was activated by incubation at 37° C. for 3½ hr., and 0·5 ml. was then added to 0·5 ml. of a solution of arginine (7 mgm. per cent) in barbital buffer at *p*H 9·6 and incubated at 25° C. for intervals ranging from 15 min. to 20 hr. The mixture was then chromatographed and the amount of arginine determined comparatively. Hyperplastic and normal skin mixed in about equal proportion were extracted and concentrated in parallel. In the experiment, the results of which are shown in Table 2, 15 gm. of combined normal and hyperplastic skin were used. In no experiment has any detectable arginase activity been found in extracts of domestic rabbit skin derived from adults or embryos in the last trimester of gestation despite the fact that much larger amounts by weight have been tested than from the Shope virus-caused papillomas, which contain this enzyme in large amounts. A trace of arginase activity has been found in wild rabbit skin extracts. However, wild rabbit skin is extremely thin and the preparation contained an estimated 25 per cent of tissue other than skin epithelium.

Table 2. COMPARATIVE ARGINASE ACTIVITY OF EXTRACTS OF PAPILLOMA AND OF NORMAL AND HYPERPLASTIC SKIN

	Arginine remaining after incubation period (per cent)		Ornithine after incubation (per cent)
	15 min.	20 hr.	
Papilloma extract	5·5	0	++++
Skin extract	120*	117*	0
Buffer plus arginine	100†	100	0

* Increase due to small amount of arginine present in concentrated dialysate.
† Equivalent to 0·07 mgm. arginine per c.c.

Only a trace of arginase activity has been detectable in a preparation of isolated and concentrated Shope virus containing 1·20 mgm. of protein nitrogen per c.c. incubated with 0·07 mgm. arginine per c.c. for 20 hr. The virus was isolated using the method of Beard, Bryan, and Wyckoff[3]. In view of the large amount of virus in this preparation, the arginase would seem most probably a contaminant rather than being an intrinsic attribute of the virus particles.

It is evident from these results that the Shope virus infection of epithelial cells is somehow inducing arginase in cells of a sort which contain no detectable arginase in their normal or hyperplastic state. One such means is that the presence of the virus in the cells induces or enables them to synthesize an enzyme new to them, arginase. Another possibility is that the virus induces a permease allowing the cells to concentrate arginine, the concentration of which in turn induces arginase. Either of these two possibilities would increase the metabolic efficiency of the cells. Might such an increase in efficiency be responsible for the overgrowth of these cells which is manifest as their neoplastic state ?

This work has been supported by a grant from the Jane Coffin Childs Fund.

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Oral Induction of Leukæmia in Mice

THE induction of leukæmia by parenteral inoculation of cell-free brain filtrates has been demonstrated[1,2]. Speculation as to the natural route of transmission of leukæmia led to the exploration of the leukæmogenic effect of whole brains and cell-free brain filtrates when given orally.

Swiss mice, approximately six weeks old, of both sexes, and *C3H* × 101 males were used. A 1 per cent concentration (w/v) of cell-free brain filtrates was prepared in the manner previously described[3], in which distilled water was used in place of physiological saline solution. The brain mince was prepared by forcing whole fresh brain through an 18-gauge needle with a syringe.

In experiment 1, Swiss mice were deprived of food and water for 24 hr. and then given cell-free brain filtrates as drinking water. Mice which received whole-brain mince were placed in individual cages and given approximately 0·5 gm. mince in a Petri

Table 1. Experiment 1

Material fed		No. leukæmic/No. fed
Brain mince	Non-leukæmic	0/25
	Leukæmic	4/25
Cell-free brain filtrate	Non-leukæmic	0/20
	Leukæmic	5/22

Table 2. Experiment 2

Material fed by intubation	No. leukæmic/No. fed
Non-leukæmic cell-free brain filtrate	0/25
Leukæmic cell-free brain filtrate	13/25

dish. Mice were allowed to eat or drink these materials for 24 hr. and then placed on regular diets. Results of this experiment are shown in Table 1.

In experiment 2 cell-free brain filtrates were prepared from the brains of *C3H* mice. *C3H* × 101 mice were lightly anæsthetized with ether. A No. 18 polyethylene tube was passed into their stomachs and through it 1 c.c. cell-free brain filtrate was injected. Results of this experiment are shown in Table 2.

In animals which developed leukæmia, the disease appeared within three to twelve weeks. Both the gross and microscopic results were similar to those previously described[1]. Identical leukæmias developed in seven out of ten mice inoculated intraperitoneally with 0·5 c.c. of the leukæmic cell-free brain filtrate used for feeding in experiment 1.

Brains of mice with orally induced leukæmia were later shown to be infective when the cell-free brain filtrate was given orally or intraperitoneally.

From the evidence presented, leukæmia in mice can be transmitted orally by either whole leukæmic brain or its cell-free filtrate. Investigators of leukæmia in mice should be aware of this possibility in the laboratory, where mice are caged together and where cannibalism occurs.

The influence of the gastrointestinal tract in the epidemiology of leukæmia remains to be elucidated.

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Experimental Colloid Goitre produced by Thiouracil

Colloid goitres, resembling those occurring endemically in man, have been produced in the hamster by an iodine-deficient diet followed by repletion with this element after epithelial hyperplasia had developed[1]. It seemed possible that if proliferative activity of thyroid epithelial cells was produced in this species by other means, such as a goiterogen, colloid accumulation might occur when the stimulus was removed. Such would be in keeping with Marine's hypothesis of the pathogenesis of colloid goitre[2]. This has proved to be the case. The occurrence of colloid goitre in animals which had received thiouracil and allowed to recover from its effects may be helpful in our understanding of the pathogenesis of endemic goitre in man in cases where absolute iodine deficiency may not be a causative factor.

Hamsters weighing 100–125 gm. were fed diets of low iodine (2·5γ/100 gm.) or higher iodine (200γ/100 gm.) content which contained 0·3 per cent thiouracil. After subsisting on these regimens for varying periods of time up to 8 weeks the goiterogen was removed from the diet, after which the animals were allowed to live for varying intervals up to 2 months. At autopsy the thyroids were weighed and examined microscopically.

Extensive hyperplasia with loss of colloid accompanied by increased vascularity occurs within the first week after thiouracil administration. This progresses for the period during which this series of animals has been observed and conforms with the findings of others in the hamster[3,4]. The changes are more marked in animals on the low iodine intake. When the drug is removed from the diet, the follicles fill up with colloid and much of the epithelium becomes flattened, although sprigs of columnar cells are found projecting into the lumens. The degree of colloid deposition is related to the antecedent hyperplasia, that is, the time the animal received the goiterogen, together with the length of repletion. The follicles increase in size from their usual average of 45μ in diameter up to 100–150μ. The weight of the glands is increased tenfold or more.

The principal reason for this communication is to direct attention to the ease and rapidity with which diffuse colloid goitre may be produced by a goiterogen in the hamster. In our experience, comparable

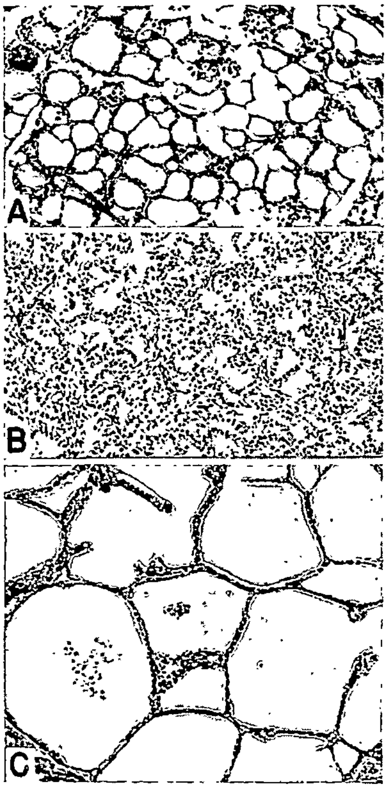

Fig. 1. Photomicrographs of thyroid glands. *A*, Normal; *B*, from an animal on low iodine–thiouracil-added diet for 20 days; *C*, from an animal comparable to *B* but off thiouracil for 3 weeks. (All × *c*. 84)

degrees of hyperplasia take a year to develop on an iodine-deficient diet[1].

Marine[5] expressed the belief fifty years ago that goitre was an iodine-deficiency disease. He viewed its pathogenesis as follows: iodine deficiency leads to hyperplasia which continues unless this element is administered; whereupon the gland fills up with excess colloid, a state representing "the nearest approach to normal glands that active hyperplasias can become". The role of the pituitary in this process is, of course, now recognized. The main difficulty in accepting Marine's hypothesis in its entirety has been that the structural alterations seen in the naturally occurring disease had not been produced in laboratory animals[6]. This is particularly true with respect to diffuse colloid goitre, although few investigators have tried to put Marine's hypothesis to the test. Most recent pathological studies on the thyroid have dealt with tumour production. Mackenzie[7] has summarized the story of experimental goitre with particular respect to the effects of iodine deficiency and goiterogenic agents, and points out that "with the judicious use of antithyroid drugs and thyroxine (or perhaps diet) we may be able to produce the elusive colloid goitre in the laboratory". Since this has been accomplished by iodine deficiency and goiterogens in the hamster it appears that pointed studies of other species, excepting perhaps the rat[7], will be of interest and throw further light on the pathogenesis of endemic goitre in man.

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Variability of Content of Deoxyribonucleic Acid in *L*-strain Fibroblasts

It is well known and has been amply demonstrated that the deoxyribonucleic acid content of normal 'resting' mammalian cells in the host is constant from cell to cell and tissue to tissue. The germinal tissue is the single exception, having instead exactly half the quantity of acid. This has been felt to reflect the constant chromosome number of these cells.

In tissue-culture cells, however, conflicting evidence is at hand. Some work apparently demonstrates a constant level of deoxyribonucleic acid, while other investigations reveal changing content of the acid depending on the cultural circumstances. Simonovitch *et al.*[1] found that in their rotating suspension cultures of *L*-strain fibroblasts, the deoxyribonucleic acid content paralleled at all times the cell number. Their cultures were always seeded from a parent culture which was in the logarithmic phase of growth. Recently, Salzman has used HeLa cells to obtain different results. He finds that during the lag phase of these cells grown as monolayers on glass, there is doubling of deoxyribonucleic acid, ribonucleic acid and protein, while the cell number does not change. On the other hand, when these cells are grown in suspension cultures, ribonucleic acid and protein but not deoxyribonucleic acid rise before the number of cells[2].

In our work with *L*-strain fibroblasts in continuous agitation suspension cultures[3], we have made some observations which incorporate these apparently conflicting data. Fig. 1 illustrates the fact that, when a subculture is made from a parent culture which is old and in the stationary phase (reflected in a stable cell population and low values of protein per cell), the content of deoxyribonucleic acid per million cells in the subculture follows a sharply rising and falling curve: during the first day, the deoxyribonucleic acid almost doubles, while cell population remains unchanged. When, on the other hand, the subculture is seeded from a parent culture which is in logarithmic growth at the time of the transplant, the daughter culture immediately goes into logarithmic growth, and content of deoxyribonucleic acid per million cells remains constant throughout the log growth period. Protein content, also shown in Fig. 1, parallels the content of deoxyribonucleic acid in both instances. A lag phase can be produced at will in any culture by adjusting initial *p*H to 7·4.

If the constant deoxyribonucleic acid level of the cells seeded from cultures in logarithmic growth represents the basic chromosomal acid-level of these cells, then it is clear that the cells seeded from stationary cultures replicate deoxyribonucleic acid to almost twice the normal complement in the 24-hr. lag phase. Apparently in these latter cells, the stimuli for replication of deoxyribonucleic acid and for division have become disordered and out of phase during the stationary period, with the result that while replication of deoxyribonucleic acid proceeds, division does not. In most normal cells, it seems clear that replication of deoxyribonucleic acid occurs during the last half of interphase[4], and if these cells were synchronous in time of division, it would appear that the accumulation of deoxyribonucleic acid merely represents this pre-mitotic replication. However, multiple mitotic counts using aceto-orcein stain have demonstrated no evidence of such synchrony in our cultures. Furthermore, the cell count increases gradually in the first 24 hr. of logarithmic growth.

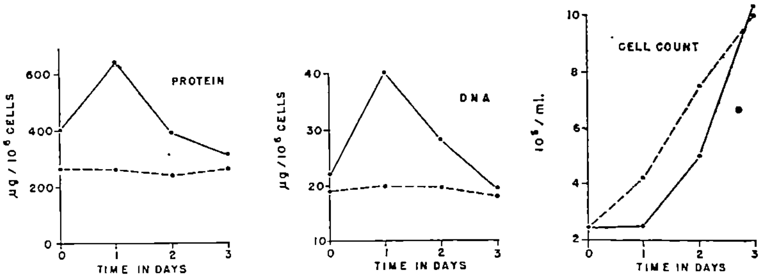

Fig. 1. Protein, deoxyribonucleic acid and cell count in fibroblast cultures. The solid lines refer to cultures seeded from parent cultures in stationary phase: the broken lines refer to cultures seeded from parent cultures in log growth phase. Each line represents the average of at least four experiments. Deoxyribonucleic acid was determined by the indole method (ref. 5), protein with phenol reagent (ref. 6) and cell number was counted in a hæmacytometer on aliquots of the undiluted medium

The results presented bring together some of the previous apparently conflicting data, and clearly support Salzman's contention[2] that deoxyribonucleic acid and protein content cannot be used indiscriminately as indications of cell number in tissue culture.

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Stress Activation of Adrenal Glomerulosa

THE experimental data concerning the hormonal regulation of adrenal glomerulosa and its mineralocorticoid production[1] are still inconclusive. The demonstrated dependence of the glomerulosa reaction on the presence of pituitary[2] as well as on adrenocorticotrophic hormone[3] is contradictory to the absence of increased aldosterone secretion by adrenals perfused with either adrenocorticotrophic or somatistrophic hormone *in vitro*[4]. Nevertheless, it can be assumed that the former, and stress, activate the adrenal glomerulosa indirectly[5], mediated by the pituitary-dependent glucocorticoid production, which becomes properly balanced by means of mineralocorticoids[6]. This view will be supplemented by further experimental results.

Adult Wistar rats, males or females, divided into three separate groups (96 animals altogether), were subjected to stress by a single intra-muscular injection of 0·3 ml. 4 per cent formaldehyde/100 gm. body-weight. At intervals of 3, 6, 12, 24, and 48 hr. rats were killed. Frozen sections of adrenals were stained with sudan black *B* and with oil red *O* on lipids. The width of the zona glomerulosa was measured at a magnification of × 330, in all four quarters of the adrenal cortex. The number of leucocytes, eosinophils, and the differential count of leucocytes were also determined; the spleen and thymus were examined histologically.

In the unstressed rats of all three series the lipid content of the zona fasciculata was relatively low, resembling that of series *B*, described previously[5]. 3–6 hr. after the formaldehyde injection a considerable decrease and even disappearance of lipids took place in the fasciculata. The lipid content of the glomerulosa, however, remained unchanged. 24–48 hr. after the injection the lipids of fasciculata were gradually restored and simultaneously the glomerulosa was activated, as judged from the depletion of their lipids and from a statistically highly significant ($P<0.001$) enlargement (Fig. 2). The glomerulosa activation was associated with the transformation of light centres of spleen lymphatic nodules, previously activated by stress, into resting ones, and with the return of neutrophils to the initial level; that of lymphocytes ($P<0.01$) and eosinophils rose above the initial level (Fig. 1).

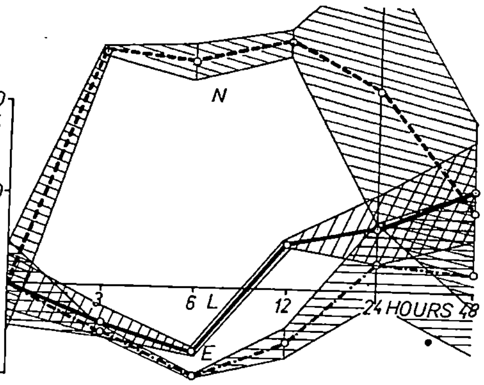

Fig. 1. The stress changes of neutrophils (*N*), lymphocytes (*L*) and eosinophils (*E*) expressed as a percentage of the mean initial value, with their standard deviations

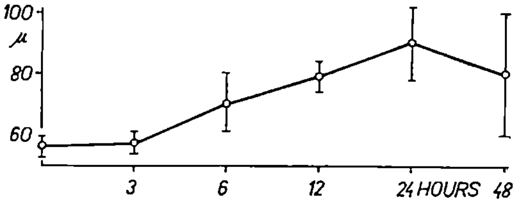

Fig. 2. The stress changes of the mean width of the zona glomerulosa in μ and their standard deviations

The findings show that the activation of the glomerulosa corresponds to changes in the leucocytes and the lymphoid tissue opposite to those found during the glucocorticoid phase of stress. Taking into account the mutual antagonism between mineralocorticoids and glucocorticoids[6], we may suppose that the activation of the glomerulosa is elicited by the antecedent glucocorticoid effects, especially their influence on electrolyte and water exchanges through the cell wall. Hence the stress reaction of the glomerulosa occurs as a balance to the glucocorticoid effects by abolishing them. The stress period can thus be divided into well-defined glucocorticoid and mineralocorticoid phases.

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Electrical Response to Illumination of the Euphausiid Crustacean Eye

We have obtained reliably reproducible measurements of the electric potentials developed in the eyes of euphausiid crustaceans during stimulation by light. Such measurements may provide an objective method for the laboratory study of vision and photoregulated behaviour in planktonic forms which undergo vertical migrations too extensive to be duplicated experimentally with any available equipment. Preliminary observations of two species from the San Diego Trough off California, and one from Loch Fyne in Scotland, are presented here.

The specimens were collected with standard plankton nets and carried to the laboratory in refrigerated polythene or glass containers filled with off-shore water. Low temperatures (2–9° C.) and darkness improved their chance of survival, and, after an initial 24-hr. recovery period, any surviving animals lived for a week to ten days.

During an experiment an animal lay on its side in a groove across the surface of a lucite disk. Silver–silver chloride gauze on the bottom of the groove served as the indifferent electrode. The groove was narrow enough to restrict movement without interfering with respiration. The plastic disk rested in a Petri dish containing just enough sea water to cover the animal in the groove. The Petri dish was surrounded by an ice bath.

The recording electrode was a piece of tungsten wire etched electrochemically to a tip of less than 2-μ diameter, and insulated down to near this tip with 'Insulex'. (The electrode was dipped in a diluted solution of 'Insulex', clamped with tip upward and dried rapidly in a gentle downward air current.) This microelectrode was attached to a plastic rod held in a ball-and-socket joint, such that the tip might penetrate the eye without blocking the light. Glass micropipettes with silver–silver chloride electrodes were used at first, but penetration of the eye with the tungsten electrodes seemed to give less damage as judged by survival time and gave identical electrical responses. The preparation was housed in a light-tight, copper-shielded box.

The light source, a 12-volt concentrated tungsten filament lamp, was situated outside the box, as were the filter holder and shutter, so that colour, intensity and duration of the stimulating flash could be altered without disturbing the preparation. The light entered the box through a baffled collimating tube, struck a concave mirror set at 45° across the light path, and was directed downward on to the exposed eye. Interference filters were used in the colour determinations, and the dimensions of the collimator were such that the useful 5° cone of these filters was not exceeded. A heavy-duty storage battery supplied power for the lamp, and the voltage across the lamp terminals was monitored throughout the experiments. Light intensity was varied with neutral density filters.

The inner surfaces of the lamp housing, filter holder, collimator and light-tight box were painted matt black.

Electrical signals from the recording electrode were fed via a cathode follower to a resistance-coupled amplifier and an ink writer or a cathode-ray oscilloscope. Control experiments were run to make sure that no artefact occurred due to photochemical properties of the electrode system. No electrical signals were detectable when the recording electrode was illuminated at the highest experimental intensity, whether simply immersed in sea water or inserted in the eye of a dead animal. Furthermore, in the absence of light on the eye, no electrical activity could be detected even when the animal exerted swimming movements.

At the outset of an experiment the room was darkened, the stimulating lamp was turned on, the shutter was opened and a deep red filter was placed in the light path. The animal was transferred quickly from the dark storage vessel to the indifferent electrode. The position of the Petri dish was adjusted such that only the eye of the subject was illuminated, and the recording electrode was inserted. The shutter and the door of the light-tight box were then closed, and the animal remained in total darkness for at least 30 min. before measurements were begun.

The response to a brief flash (100 msec.) of 'white' light of moderate intensity is shown in Fig. 1, with representative curves from (*A*) *Euphausia pacifica*, (*B*) *Nematoscelis difficilis* and (*C*) *Meganyctiphanes norvegica*. The response in each species is rapid, with a small *a*-wave lasting about 20 msec., a main response which reaches a peak in 40–50 msec., and a final overshoot in the other direction. Over a defined range of intensities the height of the main response to short flashes of light varies directly with the logarithm of the intensity of the light. At very low intensities the signal is lost in the noise, and at high intensities the signal reaches a limiting value, of the order of 200–300 μvolts.

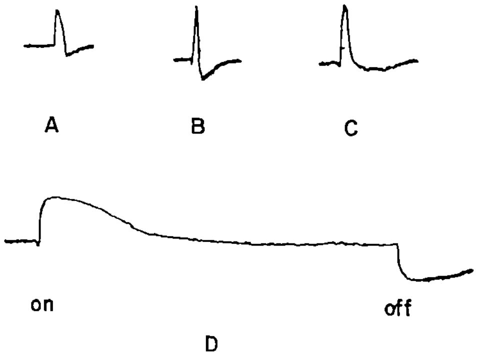

Fig. 1. Response to a 100-msec. flash of 'white' light by: (*A*) *Euphausia pacifica* (recorded with a cathode-ray oscilloscope); (*B*) *Nematoscelis difficilis* (recorded with a Beck–Lee ink writer); (*C*) *Meganyctiphanes norvegica* (recorded with an electro-encephalograph designed by Dr. Grey Walter); (*D*) response of *M. norvegica* to a 5-sec. flash

Light flashes of longer duration induce an electrical response at both on and off (Fig. 1 *D*).

Preliminary studies of response to light of various wave-lengths have been made, both for equal biological response and for equal energy of illumination. The euphausiid eye is most sensitive to blue-green light; but the spectral sensitivity curve does not coincide exactly with the spectral absorption curve of euphausiopsin, the light-sensitive pigment reported from the eyes of *Euphausia pacifica*[1].

The work on *E. pacifica* and *N. difficilis* was done at the Scripps Institution of Oceanography. The work on *M. norvegica* was done at The Laboratory, Plymouth. We should like to thank Dr. F. S. Russell, of Plymouth, and Dr. Harold Barnes, of Millport, for making the latter possible.

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Melatonin in Peripheral Nerve

Melatonin is a hormone, isolated from beef pineal glands, that lightens the colour of frog melanocytes either after injection into the frog or after *in vitro* incubation with pieces of frog skin[1]. In addition, this hormone can block and reverse the darkening actions of the melanocyte-stimulating hormones and also of adrenocorticotrophic hormone. Melatonin is a 5-hydroxyindole derivative in which the hydroxy group is blocked[2]. Its melanocyte-lightening properties are more than ten thousand times greater than those of noradrenaline, which previously was considered to be the most potent lightening agent known[3]. In our early experiments melatonin could be detected only in extracts from pineal glands and not from other tissues. With improvement in extraction techniques we have been able to identify the presence of a lightening agent that is most likely melatonin in peripheral nerves of man, monkey and cow. A detailed mapping of the location of melatonin in the nervous system has not been completed.

Sciatic nerves from human beings were collected at autopsy and stored at −10° C. until a total of 65 gm. of tissue was obtained. This material was lyophilized to give 28 gm. of dry tissue. The latter was cut into small pieces and defatted with petroleum ether in a Soxhlet extractor. 10 gm. of dry, defatted nervous tissue was obtained which was pulverized to a powder in a Waring blendor. The powder was mixed with 100 ml. water in the blendor, and the mixture was centrifuged at 15,000*g* for 30 min. The supernatant fluid was filtered and the residue extracted with 100 ml. water and centrifuged again. The combined filtrates were extracted twice with equal volumes of ethyl acetate. The ethyl acetate layer was evaporated to dryness *in vacuo*. The residue was dissolved in a mixture of 10 ml. of each layer of solution used for counter-current distribution. This solvent system was made by equilibrating 2 parts of water with 1 part of ethylacetate and 1 part of *n*-heptane. All solvents were redistilled prior to use. The dissolved residue was subjected to 29 transfers in a counter-current distribution apparatus. The contents of the tubes were pooled into four groups: 0–7, 8–14, 15–22 and 23–29. From each pooled group the organic phase plus the upper phase obtained by re-extraction of the water layer with an equal volume of ethyl acetate were combined and evaporated to dryness *in vacuo*. The four residues, each dissolved in 2 ml. ethanol, were assayed for their ability to lighten isolated pieces of frog skin. Activity was found only in material from tubes 8–14. Similar results were obtained from extracts made in the same way using collections of sciatic, femoral and brachial nerves of monkeys and spinal nerve roots of cows. Purified melatonin, when subjected to a similar counter-current distribution, is found in greatest concentration in tube 11; and there is the expected decrease in concentration as one moves in either direction away from the peak tube. Tubes 8–14 contain nearly all the melatonin. The active material from tubes 8–14 of the counter-current distribution of human nerve was put through the counter-current machine again. Tube 11 contained the highest concentration of the lightening agent. This location coincides with that expected from distributing melatonin. There was not enough material in tubes 8–14 to test with Ehrlich's reagent or to obtain a fluorescence curve. Other known lightening agents, for example, noradrenaline, adrenaline, acetylcholine, serotonin, triiodothyronine and hydrocortisone, are eliminated by the extraction procedures.

Since the solubility and biological properties of the agent obtained from nerves of human beings, monkeys and cows are identical with those of melatonin and different from those of other known lightening agents, it is likely that the active principle is melatonin.

The function of this powerful melanocyte-lightening agent in peripheral nerve is not known. It may play a part in the transmission of nerve impulses and in the pathogenesis of vitiligo and malignant melanomas.

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Effect of Enzymes on Mechanical Properties of Tissues

While investigating the effect of extending forces on the excised uterine cervix of the rat[1] we found that at the end of pregnancy the tissue showed prolonged extension at constant rate under low loads, behaving as if the collagenous framework in it was not continuous, as it is in the majority of tissues, but was one in which the ultimate links were viscous. In the course of investigating this viscous state we tried the effect of soaking the tissue in solutions containing trypsin. This was found to increase dramatically the rate of extension under constant load. Similar results were obtained from rings of skin cut from around the body-wall of newly born rats. Chymotrypsin was also tried on these and found to have the same effect as trypsin.

After excision, tissues were left overnight in the refrigerator (5° C.) in the enzyme solutions (crystalline Armour preparations, trypsin 0·5 mgm./ml., chymotrypsin 1·0 mgm./ml.) and incubated for 15 min. at 37° C. before testing. The method of using the enzymes and the concentration of trypsin were suggested to us by P. B. Medawar as suitable for detaching epidermis without killing the cells. Tissues were stretched between two parallel steel rods (stainless steel hypodermic needle tubing 0·6 mm. diam.). In the case of the cervix, one rod went through each canal, while the skin formed a belt around both rods.

Table 1. Rate of Linear Extension (percentage of l_0 per min.) under Constant Load

The number of animals is given in brackets. The estimate of variation is the standard error of the mean

	Normal	Trypsin-treated	Chymotrypsin-treated
Cervix (twenty-first day pregnancy) 50 gm. load	1·37 ± 0·33 (6)	30·7 ± 6·2 (3)	—
Skin (new born) 12 gm. load	0·038 ± 0·004 (6)	39·3 ± 10·2 (3)	4·7 ± 1·1 (3)

The tests were made in oxygenated Locke's solution, the tissues being loaded for periods up to 1 hr. and then broken by increasing the load in steps at constant intervals if they had not broken before.

Quantitative results are given in Table 1. The rate of extension under load is given as a percentage of the length at zero time (l_0) obtained by extrapolation backwards of the linear part of the curve (Fig. 1). Tension per unit cross sectional area of tissue calculated from weight of tissue for length l_0 was about 3 gm./mm.^{2} for both cervix and skin; per unit cross sectional area of collagen it was lower in the more collagenous cervix, that is, about 50 gm./mm.^{2} collagen as compared with about 200 gm./mm.^{2} collagen for skin.

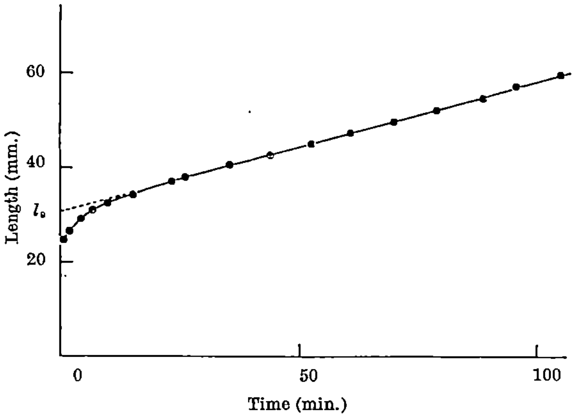

Fig. 1. Example of prolonged increase in length of tissue under constant load in cervix of rat at the end of pregnancy (twenty-first day). Length on the ordinate is that of the circumference of tissue around the rods. Load was 50 gm., giving a tension of approximately 3 gm./mm.^{2} at l_0

In contrast with the above results we have been unable so far to find any appreciable effect with hyaluronidase ('Hyalase', Benger).

Collagen itself is not attacked by trypsin or chymotrypsin, and these experiments appear to provide strong evidence that the collagenous framework is held together by some other unidentified protein on which the mechanical properties and integrity of the whole tissue depends. They strongly support the views put forward by Day[2] on the nature of the so-called 'cement substance' in connective tissue.

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Hydrolysis of Lecithin and Lysolecithin by Rumen Micro-organisms of the Sheep

Although the diet of the ruminant contains only a small percentage of complex lipids (triglycerides, phospholipids, sterols, waxes), the actual amount ingested can be considerable because of the bulk of the food eaten. Furthermore the surface activity of such lipids may play an important physico-chemical part in ruminant digestion, and recent evidence suggests that the ingested chloroplast lipids act as efficient anti-foaming agents in the rumen[1]. At the present time, little is known about the way in which these complex lipids are digested by ruminants. Recently, however, Garton, Hobson and Lough[2] have described a rapid hydrolysis of triglycerides when these were incubated with sheep rumen contents.

The present communication describes observations made over the past two years on the hydrolysis of phospholipids by sheep rumen micro-organisms. When lecithin labelled with phosphorus-32[3] was incubated with sheep rumen contents, or a washed preparation of rumen micro-organisms there was a rapid breakdown of lecithin and the phosphorus-32 label appeared in the water-soluble fraction mainly as inorganic phosphorus. Similar incubations have been performed in the presence of a series of likely metabolic intermediates of lecithin hydrolysis, for example, phosphorylcholine, glycerylphosphorylcholine, glycerophosphoric acid, in order to trap the radioactive fragment split off from the lecithin and largely protect it from further catabolism. These substances were then separated from other phosphorus compounds in the incubation medium by two-dimensional paper chromatography and their radioactivity measured both by autoradiography and also by direct radioactive assay of the digested spots. Such experiments showed that the major catabolic pathway was via glycerylphosphorylcholine and glycerophosphoric acid. At the same time there appeared to be a minor pathway via phosphorylcholine.

Washed preparations of rumen micro-organsims also hydrolysed lysolecithin, although individual animals showed wide variations in the level of activity. By autolysis of the micro-organisms or on their treatment with butanol a soluble preparation of the enzyme was obtained. This has been purified by ammonium sulphate precipitation and adsorption on calcium phosphate gel. Such preparations possess no lecithinase activity but they readily hydrolyse lysolecithin producing glycerylphosphorylcholine. Lysophosphatidyl ethanolamine is also attacked. The *p*H optimum in collidine–hydrochloric acid buffer is 7·5, which is different from the *p*H optima of the lysolecithinases of animal tissues (6·0) and moulds (3·3–4·0). In buffers containing alkali metals, for example sodium glycine–glycine, the activity was much greater at high *p*H's (7·5–9·5) than in buffers with organic bases. The enzyme does not appear to need any metal ion for activation, and it is not appreciably affected by ethylenediamine tetraacetic acid. It is comparatively insensitive to inhibition although copper and zinc ions are effective, as is also 0·01 per cent cetyltrimethylammonium bromide.

No information has been obtained as to the identity of the organism(s) responsible for the phospholipid hydrolysis. Cultures of mixed rumen streptococc grown in a glucose rumen–liquor medium possessed little lysolecithinase activity. Hayaishi and Kornberg have reported that a soil bacterium *Serratia plymuthicum* can metabolize lecithin via glycerylphos phorylcholine while the hydrolysis of lecithin to phosphorylcholine (lecithinase *C*) by some members of the *Clostridium* genus is well known[5,6]. Recently, *Bacillus cereus* has also been shown to contain a lecithinase *C*[7].

The level of lysolecithinase in the rumen micro-organisms seems to be dependent upon the diet of the animal. Nevertheless the presence of phospholipid in the food did not appear to be essential, as an animal receiving a synthetic diet of cellulose and mineral salts with a minimum hay supplement (15 per cent) still retained considerable lysolecithinase in its rumen micro-organisms. It is interesting, however, that in these circumstances the enzyme was no longer solubilized by autolysis of the micro-organisms although butanol treatment was effective.

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Bilirubin Metabolism in the Fœtus

It has been shown that in fœtal liver the enzymatic mechanism for glucuronide formation is poorly developed, while a rapid increase in enzymatic activity occurs during the early neonatal period[1]. The transient hyperbilirubinæmia observed during the first few days of life is believed to be related to this inadequate development of the hepatic conjugating system[1]. Since a significant increase in serum bilirubin concentration usually occurs only after the cord is severed, it has been assumed that during gestation the placenta is responsible for the removal of fœtal bilirubin. It has not been determined, however, whether the placenta has the ability to conjugate the fœtal pigment or whether placental transfer of unconjugated bilirubin occurs from the fœtal to the maternal circulation.

In vitro, glucuronide formation was studied[2] both with human placenta obtained at term or by Caesarean section and with rat placenta at various stages of gestation. Incubations were carried out with tissue slices, homogenates and microsomal preparations in the presence of UDPGA, using as substrates bilirubin, *o*-aminophenol and *p*-nitrophenol[2]. In these systems, no evidence for glucuronide formation was obtained. Moreover, supravital perfusion of human placenta[3] failed to reveal formation of bilirubin glucuronide.

In view of these negative results, placental transfer of bilirubin was studied in pregnant guinea pigs during the last week of gestation using a modification of the method described by Dancis *et al.*[4]. On the maternal side, a uterine vein was cannulated which permitted continuous sampling of venous blood from an individual placenta. The corresponding fœtus was delivered into a saline bath, maintained at 37° C., and an umbilical artery was cannulated, while the umbilical vein was severed and the cord clamped proximal to the fœtus. Over a period of 1 min., 0·4 mgm. crystalline bilirubin, dissolved in 1 ml. of either 5 per cent human albumin or guinea pig plasma, was infused through the cannulated umbilical artery. In addition, the injected solution contained either iodinated human albumin (2,500,000 counts/min./ml.) or chromated guinea pig erythrocytes (3,000,000 counts/min./ml.). Blood samples from the uterine vein were taken before, during and at various time-intervals after the injection for estimation and paper chromatography[5] of bilirubin and for determination of the radioactivity in albumin and in erythrocytes.

The injected bilirubin was rapidly transferred through the placenta and was present in the maternal blood as non-conjugated bilirubin. Peak concentrations ranging from 0·6 to 2·0 mgm. per cent were reached in the uterine venous blood 2–4 min. after the beginning of the injection. As seen in Fig. 1, iodinated albumin was transferred at a rate similar to that of bilirubin. On the other hand, no radioactivity was detected in the maternal blood if bilirubin was injected together with chromated erythrocytes. Similarly, injection of crystalline bilirubin into the maternal circulation resulted in its rapid appearance in the fœtal blood. Conversely, if bilirubin glucuronide obtained from human bile and iodinated albumin were injected into the umbilical artery, transfer of conjugated bilirubin was minimal, while radioactive albumin rapidly appeared in the maternal blood.

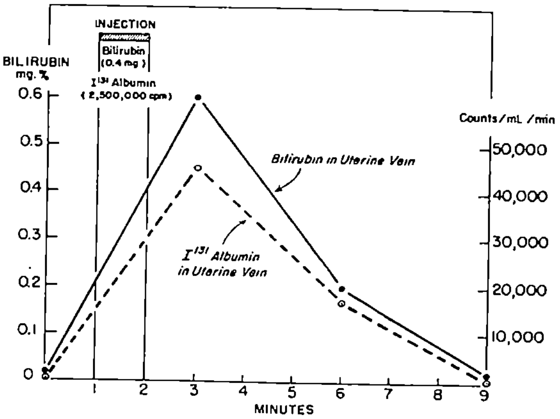

Fig. 1. In a pregnant guinea pig shortly before term, 0·4 mgm. bilirubin and albumin labelled with iodine-131 (2,500,000 c.p.m.) were injected into a fœtal umbilical artery. Concentrations of bilirubin and radioactive albumin were determined in the corresponding uterine vein

These observations indicate that under the experimental conditions employed, non-conjugated bilirubin was rapidly transferred from the fœtal to the maternal circulation, while transfer of conjugated bilirubin was insignificant. They are in agreement with the findings of Dancis *et al.*[4] that œstrogens but probably not œstrogen glucuronides can pass the placental barrier. In view of these findings, the possibility was considered that the inadequate development of the mechanism for glucuronide formation in the fœtal liver may be due to a lack of substrate during the intra-uterine period. This problem was studied by injecting six pregnant rats with large amounts of anthranilic acid, a compound which is largely excreted as an acyl-glucuronide[6]. During the last six days of gestation, 50 mgm. sodium anthranilate/100 gm. body-weight were injected twice a day by intraperitoneal route and a

Table 1. EFFECT OF INJECTION OF SODIUM ANTHRANILATE ON THE BIOSYNTHESIS OF *o*-AMINOPHENYL GLUCURONIDE BY MICROSOMES OF MATERNAL AND FŒTAL RAT LIVERS *in vitro*

Type of treatment and No. of animals	*o*-Aminophenyl glucuronide formed	
	Mother	Fœtus
Saline (control), 6	0·044 ± 0·013	0·008 ± 0·005
Anthranilate, 6	0·041 ± 0·019	0·011 ± 0·003

Washed microsomes obtained from 1 gm. of liver were incubated for 30 min. at 37° C. with 0·2 μmole *o*-aminophenol, 1 μmole UDPGA and 25 μmoles magnesium chloride in 0·1 *M tris* (hydroxymethyl) amino-methane buffer, *p*H 8·0. Results are expressed as μmoles formed per gram of liver ± standard deviation

similar group of pregnant rats was given a comparable amount of saline. 12 hr. after the last injection, the animals were decapitated, and microsomes were prepared from the fœtal and maternal livers. In mothers treated with anthranilate, fœtal liver exhibited anthranilic acid concentrations[7] of 18·3 μgm. (*S.D.* 5·9 μgm.) per gm. tissue, while none was detectable in maternal livers or in fœtal livers of saline-treated mothers. Washed microsomes obtained from 1 gm. of liver were incubated with *o*-aminophenol and UDPGA and the amount of *o*-aminophenyl glucuronide formed was estimated[2]. As seen in Table 1, no difference in glucuronide formation was observed between microsomal preparations of fœtal livers that were obtained from mothers treated with anthranilate or with saline. Moreover, the magnitude of glucuronide formation by microsomes of maternal livers was similar in both groups of rats. Per gm. of liver, fœtal microsomes exhibited about four times less enzymatic activity than maternal preparations; but if the values were expressed per mgm. of microsomal protein nitrogen, this difference was much smaller. This is believed to indicate that on a weight basis fœtal liver may contain less precipitable microsomal particles than adult liver.

The results suggest that in fœtal rat liver increased activity of the glucuronide-forming enzyme system cannot be induced by the presence of substrate, even though the aglycone is present in considerable concentration over the last five days of gestation. Other factors must be responsible for the 'immaturity' of the fœtal liver. To what extent these observations may be applicable to man remains to be elucidated.

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Flavone Glucosiduronic Acids in *Scutellaria* sp.: a Correction

IN the course of studies on the isolation of flavone glucosiduronic acids from various skull-caps, specimens of a localized colony at Mells, Somerset, which had been identified as *Scutellaria columnae* Tenore[1], were reported[2] to contain scutellarin (5,6,7,4′-tetrahydroxyflavone β-glucosiduronic acid) and not baicalin (5,6,7-trihydroxyflavone β-glucosiduronic acid) as found previously[3] in this species grown in the area of Paris. This anomaly is now removed by the recent re-identification[4] of the Mells skull-cap as *Scutellaria altissima* L., a native of south-east Europe. Scutellarin was originally isolated from this plant[5].

Thanks are due to Dr. A. J. Willis for directing my attention to this reclassification.

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Relationship between Auxins and Nucleic Acid Synthesis in Coleoptile Tissues

THAT auxins may affect nucleic acid metabolism in plants has been suggested by a number of workers. Silberger and Skoog[1] had observed an increase in both the deoxyribonucleic acid and ribonucleic acid content of tobacco pith cells incubated with 0·01 to 10 mgm./l. of indole acetic acid. Growth continued in a manner somewhat similar to changes in the ribonucleic acid content for a few days even though the synthesis of nucleic acids had apparently stopped after four days of application of indole acetic acid. Holmes *et al.*[2] have shown that in *Vicia* root, as the distance from the root tip increased the content of deoxyribonucleic acid per cell also increased. Attempts have been made to correlate root growth with nucleic acid metabolism in other plants as well[3-5]. In maize roots it has been found that application of indole acetic acid resulted in a slowing down of growth accompanied by a decrease of both deoxyribonucleic acid and ribonucleic acid[3]. Some workers are inclined to believe that growth and synthesis of deoxyribonucleic acid in plants continues only in the presence of auxins[6-8]. The present communication summarizes the results obtained in an investigation on the incorporation of compounds labelled with phosphorus-32 and carbon-14 into the coleoptile tissues as affected by indole acetic acid.

Seeds of *Avena sativa* var. *N.P.*1 and *Oryza sativa* var. Rupsail were used. The seeds were germinated in the dark with occasional red light for 3 days. The coleoptiles were then decapitated at 2–3 mm. and floated on water for 2 hr. to free them from any endogenous auxin. After a further decapitation by another 2–3 mm., 5-mm. sections were cut off and floated on the experimental solution containing $Na_2H^{32}PO_4$ (50 μc./ml.) of specific activity greater than 1 mc./μgm. phosphorus in *M*/150 phosphate buffer of *p*H 6·0 for 2 hr. with or without indole acetic acid. For rice, 5-day old coleoptiles were used. ($Na_2H^{32}PO_4$ was obtained from N.V. Philips Roxane

Table 1. THE EFFECT OF INDOLE ACETIC ACID ON INCORPORATION OF PHOSPHORUS-32 IN THE NUCLEIC ACIDS OF RICE (VAR. RUPSAIL) COLEOPTILES

Results expressed as counts/min. in the nucleic acid per mgm. of coleoptile × 10^{-3}

Treatment	Ribonucleic acid	Deoxyribonucleic acid
Control	426·6	296·5
10^{-6} *M* indole acetic acid	632·6	387·4

Pharm.-Chem. Industrie Netherlands.) After the end of the incubation period, cold trichloracetic acid was added and the nucleic acids fractionated according to the method of Ogur and Rosen[9]. Measurements of radioactivity were taken with a Nuclear Chicago halogen counter coupled with a Tracerlab autoscaler.

The results are presented graphically in Fig. 1. With low concentration of indole acetic acid there is a marked stimulation of incorporation of phosphorus-32 into both deoxyribonucleic and ribonucleic acid fractions. In the latter, a concentration of 10^{-9} *M* indole acetic acid has practically no effect; but 10^{-6} *M* has a distinct stimulatory effect, the increase observed being more than 50 per cent. In the former, the rate of incorporation of phosphorus-32 is much slower, and the maximum increase observed due to the application of indole acetic acid was 20 per cent. With 10^{-3} *M* indole acetic acid there appears to be an inhibition in the incorporation of phosphorus into deoxyribonucleic acid. Similar stimulation of incorporation of phosphorus-32 due to low concentrations of indole acetic acid was also observed when rice coleoptiles were incubated with 125 μc./ml. of $Na_2H^{32}PO_4$ in phosphate buffer with and without 10^{-6} *M* indole acetic acid.

To study the utilization of compounds labelled with carbon-14 for nucleic acid synthesis the coleoptiles were incubated with the following compounds (obtained from the Radiochemical Centre, Amersham, Great Britain) in *M*/165 phosphate buffer of *p*H 7·0 with or without 10^{-6} *M* indole acetic acid: (1) sodium acetate-1-^{14}C (37 μgm./μc.)—45 μc./ml.; (2) acetate-2-^{14}C (14·9 μgm./μc.)—9 μc./ml.; (3) $NaH^{14}CO_3$ (3·7 μgm./μc.)—45 μc./ml.; (4) sodium formate-^{14}C (14·1 μgm./μc.)—45 μc./ml.; (5) glycine-1-^{14}C (22 μgm./μc.)—10 μc./ml. When the nucleic acids were extracted and isolated as described above no stimulation of incorporation of carbon-14 was observed in both ribonucleic and deoxyribonucleic acids, with the exception of glycine.

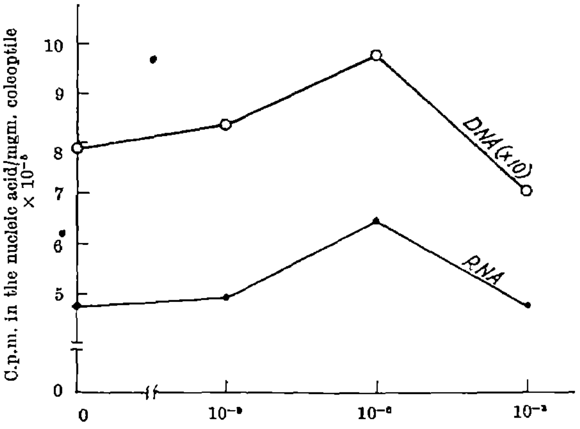

Fig. 1. Effect of indole acetic acid on the incorporation of phosphorus-32 into the nucleic acids of *Avena* coleoptile. The values for deoxyribonucleic acid have been multiplied by 10 for clarity

It thus appears that the effect of auxins on nucleic acid synthesis during the first 2 hr. of application is exercised through its effects on the synthesis of nucleotides composing the nucleic acids. That indole acetic acid stimulates the synthesis of nucleotides and phosphorylation reactions has now been confirmed with compounds[10] labelled with phosphorus-32, as also through the recent work of Marre[11]. The compounds labelled with carbon-14 used are all known to contribute to the synthesis of purine and pyrimidine bases of the nucleic acids. Apparently during the first 2 hr. of application of indole acetic acid the reactions leading to their synthesis or of the sugar moieties of the nucleic acids are not much affected, even though the phosphorylation reactions are.

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BACTERIOLOGY

Neutralization of Bacteriophage by Normal Serum

NORMAL mammalian serum of most species is capable of neutralizing bacteriophages of the *Escherichia coli T* series. This activity of normal serum has been attributed to the properdin system although a lack of correlation between properdin-levels and phage-neutralizing activity was noted with certain sera[1]. Recent work by Cowan[2], moreover, in which several human sera were assayed for activity against *T*2, *T*6, and *T*7, indicated that the phage-neutralizing activity of a serum against one of the phage types was not correlated with its activity against the other two. These results suggested that the properdin system, essentially non-specific in its action, could not adequately account for the activity of normal serum against the three phage types. Cowan postulated, therefore, that properdin might be a family of cross-reacting antibodies capable of combining with zymosan. Similar considerations are applicable to other activities of normal serum. Our own findings in studies of the bactericidal action of normal serum against several species of Enterobacteriaceae indicated that bactericidal antibody of marked specificity plays the major part[3].

A more direct demonstration of the significance of normal antibody of marked specificity, as opposed to properdin, in the phage-neutralizing activity of normal serum was obtained in our laboratory.

Escherichia coli bacteriophage $T2$ was prepared and concentrated as described by Herriot and Barlow[4]. High-titred cultures of phage $T5$ were obtained by using the procedure outlined by Adams[5]. Phage-*E. coli* complexes were prepared by the addition of bacteriophage concentrates $T2$ or high-titred broth cultures $T5$ to 100 ml. aliquots of tryptone broth cultures of *E. coli* B (at least 3 days old) at 37° C. The cultures then contained approximately 25 infective phage particles per bacterium. After 1–2 min., formalin was added to inactivate both phage and bacteria. After 3 hr. at room temperature, the bacteria with attached phage were centrifuged in the cold. When $T2$ was used, the bacteria formed a highly viscous residue which was washed twice with saline. This viscosity was due to the deoxyribonucleic acid in the residue. Digestion of this acid was accomplished by the addition of 10 ml. of 0·15 *M* sodium chloride solution, 0·1 ml. of 0·028 *M* magnesium sulphate solution and 10 μgm. of deoxyribonuclease (Worthington Biochemical Corp.). The enzyme was allowed to act overnight at room temperature. This treatment was sufficient to allow resuspension of the bacteria with attached phage, which were sedimented by centrifugation prior to the addition of serum. With $T5$, the bacteria formed a residue easily resuspended in saline. Digestion with deoxyribonuclease was therefore not required. The *E. coli*-$T5$ complex was washed three times with saline prior to the addition of serum. As a control, *E. coli* cells without phage were similarly treated with formalin and saline. Each serum (10 ml.) was adsorbed twice with either the *E. coli*-$T2$ or *E. coli*-$T5$ preparations for 1 hr. at 0° C. An aliquot was similarly treated with the control *E. coli* cells.

Phage-neutralizing activity titres of adsorbed and unadsorbed sera using homologous and heterologous bacteriophage are summarized in Table 1. Adsorption of normal serum with *E. coli*-phage complex resulted in almost complete removal of phage-neutralizing activity when tested against the homologous phage. In contrast, when this adsorbed serum was titrated against heterologous phages in the T-series, phage-neutralizing activity was essentially equal to that of the unadsorbed serum. This indicates that the component essential for the neutralization of phage by normal serum is a substance characterized by marked specificity. It is also interesting to note that the serum adsorbed with $T2$ phage and titrated against $T4$ and $T6$, both serologically related to $T2$ [6], had about 50 per cent of the phage-neutralizing activity of the untreated serum. Conversely, the same serum, when tested against serologically unrelated phage, showed only slight diminution of activity as compared with the neutralization by the untreated serum.

Table 1. NEUTRALIZATION OF HOMOLOGOUS AND HETEROLOGOUS BACTERIOPHAGE BY ADSORBED AND UNADSORBED NORMAL HUMAN SERUM

Serum No.	Phage-neutralizing activity titre* against: $T2$	$T4$	$T6$	$T5$	$T7$
120858 Untreated	23	7	65	10	16
120858 Adsorbed with *E. coli*-$T2$	<1	3·3	37	9·5	15
20959 Untreated	22	11	51	16	25
20959 Adsorbed with *E. coli*-$T5$	19	6	46	<1	23

* The reciprocal of the amount of serum (ml.) required to neutralize 50 per cent of about 10^3 phage particles in a total volume of 1 ml. at 37° C. for 1 hr. Serum and phage were diluted in veronal buffer containing 0·1 per cent bovine serum albumin (ref. 2).

Table 2. COMPLEMENT, PROPERDIN AND PHAGE-NEUTRALIZATION (PNA) TITRES OF UNADSORBED AND ADSORBED NORMAL HUMAN SERUM

Human sera	Serum No. 120858			Serum No. 20959		
	PNA titre against $T2$	Complement units*	Properdin units†	PNA titre against $T5$	Complement units*	Properdin units†
Untreated	23	240	12	16	230	12
Adsorbed with *E. coli* cells	19	216	4	14	230	6
Adsorbed with homologous *E. coli*-T phage complex	<1	180	4	<1	192	6

* The reciprocal of the dilution of serum required to hæmolyse 50 per cent of the sensitized sheep erythrocytes ($1 \cdot 5 \times 10^8$ cells) in a total volume of 1·5 ml. at 37° C. for 30 min. Triethanolamine buffered saline was used as diluent.

† Euglobulin precipitates dissolved in endpiece were assayed as described (ref. 8).

Studies of the adsorbed and unadsorbed sera were undertaken to characterize further the serum components responsible for this activity against phage. Since the properdin system has been suggested as the factor in normal serum required for phage neutralization[7], it was necessary to measure the complement- and properdin-levels in adsorbed and unadsorbed sera. The complement titres in Table 2 indicate a slight loss in hæmolytic complement as a result of the adsorption. The slight reduction in phage-neutralizing activity against heterologous phage types seen in Table 1 may be related to this complement loss. From the properdin and phage-neutralizing activity titres in Table 2, it can be seen that adsorption with *E. coli* cells alone resulted in a 2–3 fold reduction in properdin with a scarcely detectable decline in phage-neutralizing activity. The results in Table 2 also indicate that the attached phage particles are not responsible for any detectable loss of properdin. Of greater significance, however, the phage-neutralizing activity is markedly reduced in the serum adsorbed with homologous phage despite the presence of the properdin system components. Only very slight reduction in activity occurred in the serum adsorbed with *E. coli* cells alone. Yet the properdin-levels in both adsorbed sera were the same and were within normal limits. The results indicated that sera adsorbed with homologous phage but having components of the properdin system were incapable of phage neutralization. Normal antibody, removed by adsorption with the homologous phage, appeared indispensable.

The origin of normal antibodies to phage, or to any microbe, is not readily determined. That some normal antibodies are specific does not necessarily favour any particular theory concerning their origin. It merely means that they react with certain organisms, and not with others, because of a chemical correspondence of certain specific combining groups. The pooled sera of 6 germ-free 6-week-old guinea pigs possessed greater phage-neutralizing activity against $T2$ (titre equal to 33) than the sera of conventional guinea pigs (titre equal to 18) of the same strain and age. Hæmolytic complement- and properdin-levels of the two pools did not differ. Of course, germ-free animals are not necessarily free from viruses and are subjected to a variety of antigenic materials from sterile foods and viruses which may possess antigenic groupings cross-reactive with those of the T-phages. Thus, the possibility that phage-neutralizing activity resulted from antigenic stimulation in these germ-free animals cannot be excluded. The globulin-levels of the germ-free animals tested were considerably below normal, however, and the gamma fraction was scarcely detectable by paper electrophoresis.

Properdin has been described as a single substance capable of neutralizing viruses and destroying certain abnormal red cells and bacteria[9]. The results of our experiments indicate that normal antibodies of marked specificity, rather than properdin or other non-specific substances, are essential requirements for phage-neutralizing activity. In the presence of antibody, properdin may conceivably augment the existing phage-neutralizing activity.

An experiment by Bordet[10] in 1899 led to a similar conclusion. The question was raised at that time whether the activities of normal serum could be explained by one substance, or a few substances. Bordet adsorbed normal horse serum with cholera vibrios, and after removal of the cholera vibrios with attached agglutinins by centrifugation the serum lost its ability to agglutinate cholera vibrios but clumped typhoid bacilli as intensely as the unadsorbed serum.

We wish to thank Drs. M. Forbes and S. Formal for the germ-free animal sera obtained from the Germ-free Research Project, Walter Reed Army Institute of Research. We also wish to thank Mr. W. Spilman of the Division of Immunology, Walter Reed Army Institute of Research, for his suggestions in the preparation of concentrated $T2$ phage suspensions.

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Spermine as a Protective Agent against Osmotic Lysis

Previous studies have revealed a close relationship between the growth requirement of *Pasteurella tularensis* and *Neisseria perflava* for spermine or allied polyamines and their marked osmotic fragility[1,2]. The susceptibility of those bacteria to the osmotic environment is manifested by leakage of cell material, rapid decay of respiratory ability and a sharp decline of viability following their brief exposure to distilled water. In the case of *P. tularensis* the osmotic cell damage is largely prevented by microgram amounts of spermine. On the other hand, the dependence of *N. perflava* on spermine as an essential growth factor in a chemically defined medium can be eliminated by proper adjustment of its tonicity.

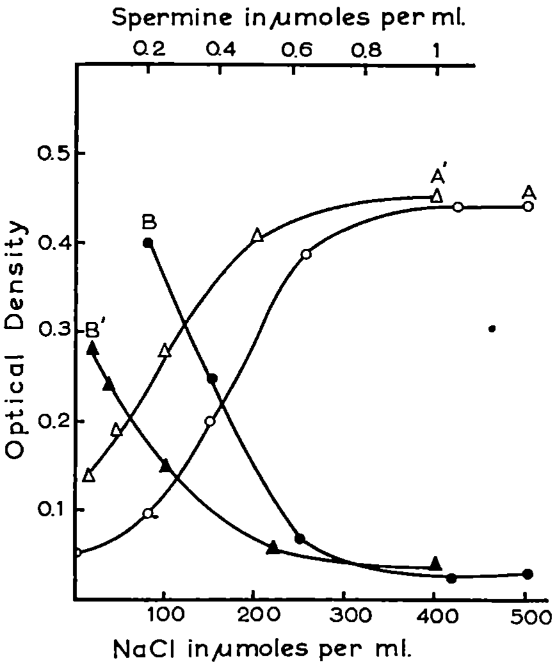

Fig. 1. Comparison of the protective effect of sodium chloride and spermine against osmotic lysis of *Achromobacter fischeri*. Washed cells of *A. fischeri* (about 3 mgm. protein content) were suspended in 1-ml. amounts of a 3 per cent sodium chloride solution supplemented with spermine in amounts corresponding to those indicated in the figure. At the end of 15 min. incubation the cells were spun off and resuspended in 5-ml. samples of the various sodium chloride or spermine solutions tested. After additional 30 min. incubation the extent of lysis was determined by measuring the turbidity of the suspensions and the absorbance of the supernates following centrifugation. Incubation temperature, 28° C. Curves *A*, *A'* and *B*, *B'* represent turbidity of the suspensions at 550 mµ and absorbance of the supernates at 260 mµ in the various sodium chloride and spermine solutions respectively (see text)

The present communication reports on the ability of spermine to prevent osmotic lysis in the obligate halophilic species, *Achromobacter fischeri* (A.T.C.C. 7744).

This organism is perfectly stable when suspended in the standard 0·5 M sodium chloride solution. It starts disintegrating, however, as soon as the osmotic strength of the suspending medium is diminished down to a critical level of about 0·25 M sodium chloride, below which the extent of cytolysis progresses in a roughly proportional manner to the decrease of osmolarity (Fig. 1). The cell rupture is evidenced by a drop in the turbidity of the suspension (curve *A*), as well as a concomitant increment in the absorbance of the cell-free supernate following centrifugation (curve *B*). The rise in optical density of the supernate is obviously attributable to leakage of cell constituents and the strong maximum exhibited close to 260 mµ is indicative of a large share of nucleotidic material.

The drastic lysis of *A. fischeri* which occurs in distilled water could be completely suppressed by adding 0·0005 M spermine provided that the cells have been pre-incubated with a similar amount of spermine while suspended in the standard sodium chloride solution. Graded amounts of spermine afforded, within a certain range of mounting concentrations, increasing protection against osmotic lysis, a definite effect being still perceptible with a quantity as low as 5 µgm./ml. (curves *A'*, *B'*). Putrescine and spermidine, known biosynthetic precursors of spermine[3], when tested under similar conditions, proved to be practically inert in the present system.

Attempts to grow *A. fischeri* in a 1 per cent peptone medium (freed by 'Norit *A*' treatment of its spermine content) devoid of sodium chloride but supplemented with spermine, were unsuccessful. Preliminary experiments, however, indicate that spermine exerts a definite growth furthering effect in combination with osmotically inadequate concentrations of sodium chloride (0·5 per cent).

The mechanism whereby spermine in these relatively minute amounts imitates the osmotic effects of salts is now being explored. A possible interplay with nucleic acids is suggested by the pronounced cationic characteristics of the compound and also by some reported interactions of apparent biological significance[4,5]. It may be concluded, therefore, that the present observations appear to bear out in a rather striking fashion the previously postulated role of spermine as a factor influencing cellular permeability[1,2]. Furthermore, some preliminary findings with a number of additional organisms suggest that the 'osmomimetic' function of this rather ubiquitous polyamine[6] may be of much wider applicability than hitherto anticipated.

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Phagocytosis of *Escherichia coli* Protoplasts

This communication reports the results of experiments on phagocytosis of the bacterial protoplasts prepared from *Escherichia coli* B, and on phagocytosis of bacterial vegetative forms obtained from these protoplasts by reversion.

The protoplasts were prepared by Lederberg's penicillin method[1]. Before each experiment the protoplasts were washed free of saccharose with physiological saline.

Both protoplasts and vegetative forms of *E. coli* were used for phagocytic tests made with horse leucocytes. The phagocytic reactions were carried out in various media, namely, in fresh undiluted serum, in fresh diluted (1 : 10) serum, in undiluted serum inactivated for half an hour at 56° C., and in inactivated diluted serum (1 : 10). The phagocytic indices were thus determined, both in the presence and in the absence of thermolabile components of complement. Such experiments afford an opportunity for discovering possible differences in the degree of phagocytosis of normal vegetative forms and of protoplasts, depending on the presence or absence of complement and fresh serum. The diluting of serum was necessary to avoid inhibition of the degree of phagocytosis. Such inhibition occurs in the phagocytic reaction with *E. coli*.

The phagocytic indices were determined by the method of Skurski *et al.*[2] without prior sensitization; the time of phagocytosis was 20 min. Comparison of the phagocytic indices afforded a measure of the phagocytosis of both vegetative forms and protoplasts. According to Wright's definition[3], the phagocytic index is the average number of bacterial cells phagocytized by one leucocyte (100 leucocytes were counted in each preparation).

The results are presented in Table 1. They show the existence of large differences in the degree of phagocytosis, the phagocytic indices obtained with protoplasts being significantly lower than those obtained with mother cells. Photomicrographs showed that protoplasts within leucocytes (phagocytized protoplasts) were swollen, whereas the shape of protoplasts outside the leucocytes were similar to those in control preparations.

Table 1. Phagocytosis of Protoplasts and Normal Forms of *E. coli* B, and of *E. coli* B Cells obtained by Reversion of Protoplasts

Phagocytized cells	Phagocytic indices			
	Normal serum		Inactivated serum	
	Undiluted	Diluted 1 : 10	Undiluted	Diluted 1 : 10
E. coli B (normal forms)	12·0	19·3	23·2	13·9
Protoplasts	1·9	5·0	9·5	4·7
Protoplasts after 6 hr. incubation	11·0	22·0	24·4	10·0
Protoplasts after 24 hr. incubation	10·0	19·0	23·3	9·5

Lederberg[1] reports that in favourable conditions reversion of protoplasts to the mother forms may occur. We have investigated this phenomenon in relation to phagocytosis. Reversion occurred in broth at 37° C. It is evident from Table 1 that after 6 hr. incubation of the protoplasts at 37° C. in broth, the phagocytic indices returned to the values obtained in control tests with mother cells. The differences in the values of the phagocytic indices of vegetative forms and of protoplasts were independent of the medium in which the phagocytic reaction occurred.

The protoplasts were much less readily phagocytized both in the presence of fresh serum (containing all the active components of complement), and in inactivated serum (containing inactivated thermolabile components of complement).

According to Park and Strominger[4], penicillin inhibits the biosynthesis of bacterial cell walls giving the protoplasts. The present communication indicates that the removal of cell walls leads to significant inhibition of the phagocytic reaction.

Prolongation of incubation times up to 24 hr. failed to change the phagocytic indices. Typical vegetative forms were observed after incubation for 24 hr., whereas after 6 hr. incubation both vegetative forms and protoplasts appear. Neither reversion nor phagocytic indices changes were observed with protoplasts stored at 2° C. in physiological saline and 20 per cent saccharose for several days.

This investigation is being continued, and the details will be published elsewhere.

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Production of Bacterial Mutants with Nitrous Acid

Recently, Mundry and Gierer[1] used nitrous acid to produce mutants of tobacco mosaic virus by chemical alteration of its ribonucleic acid, as demonstrated by Schuster and Schramm[2]. This communication deals with the mutagenic effects of nitrous acid on living cells of the bacterial species *Escherichia coli* and *Salmonella typhimurium*, the genetic substance of which is deoxyribonucleic acid.

Nitrous acid inactivates bacterial cells, reducing the ability of a suspension to form colonies. In the experiments described here, the rate of inactivation varied with differences in the state of metabolism of the cells. Those with active metabolism gave higher rates of inactivation per unit time than cells which were in a resting phase. The inactivation of such resting cells, which have only one nucleus, followed a double-hit curve (Fig. 1). Starting with about 10^8 cells per ml. its slope was tested for four logarithmic cycles of the ordinate.

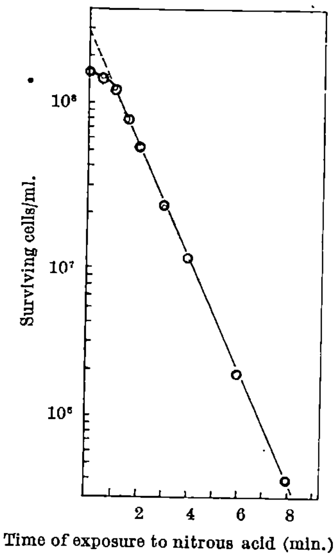

Fig. 1. Sensitivity of resting cells of *E. coli*, strain *B*, to 0·017 *M* nitrous acid (*p*H 4·5)

Wild-type cells of *E. coli*, strain *B*, which had survived treatment with nitrous acid, were plated on nutrient agar so as to give about 150 colonies per plate. Their synthetic abilities were tested by replica-plating[3] the colonies on minimal medium. Since this medium contained only glucose and inorganic salts, it supported growth of the wild-type strain but inhibited the multiplication of cells which had mutated to auxotrophy. Using this technique, auxotrophic mutants induced by treatment with nitrous acid were found. By means of a method published elsewhere[4] the mutants were tested for their growth requirements.

Details of the experiments and conclusions drawn are as follows.

(1) Nitrous acid is a potent mutagen: with an inactivation-rate of 10^{-5} about 4 per cent of surviving cells were auxotrophic mutants.

(2) The spectrum of mutants (Table 1) induced by nitrous acid differs significantly in some respects from that observed after induction with ultraviolet, other mutagens or after spontaneous origin. It is identical with the spectrum of mutants found after induction by disintegration of incorporated phosphorus-32 [4]. The most striking features are the very rare occurrence of mutants blocked in the synthesis of glycine, glycine or serine and cysteine; and the rather high frequency of purine- and pyrimidine-less mutants mainly of the cytosine- or uracil-less type as well as of the argine-less type.

Table 1. Distribution Pattern of Nutritional Requirements found in Auxotrophic Mutants induced by Incubation of Wild-Type Cells of *E. coli*, Strain *B*, with Nitrous Acid

Nutritional requirements tested	No. of mutants found	Nutritional requirements tested	No. of mutants found
Adenine	21	Proline	11
Adenine or guanine	2	Proline or glutamic acid	1
Guanine	4	Serine	2
Cytosine	0	Threonine	9
Cytosine or uracil	17	Tryptophane	28
Thymine	2	Tyrosine	9
Arginine	55	Valine	17
Aspartic acid	2	Ascorbic acid	0
Cysteine	30	Nicotinic acid	13
Cysteine or methionine	10	Pantothenate	0
Glutamic acid	3	Pyridoxal-phosphate	2
Glycine	4	Pyridoxal-phosphate or glutamic acid	1
Glycine or serine	2	Riboflavin	0
Histidine	37	Riboflavin or nicotinic acid amide	3
*iso*Leucine	9	Other unanalysed requirements	224
*iso*Leucine or valine	1		
Leucine	15		
Lysine	10		
Methionine	23		
Phenylalanine	1		

(3) The production of auxotrophic mutants in the range tested (4 per cent of surviving cells were auxotrophs) follows a double-hit curve (Fig. 2).

(4) When suspensions are used the cells of which are in different metabolic states, the percentage of mutants induced by nitrous acid is independent of

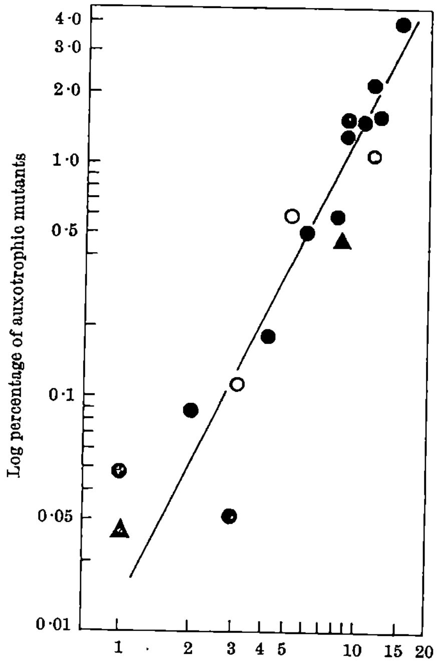

Fig. 2. Relationship between the percentage of induced mutants and the time of incubation with 0·017 *M* nitrous acid (*p*H 4·5). Since the plot is a straight line with a slope of about 60° when both axes have the same logarithmic scale the curve is evidence for a double-hit reaction. ●, Resting cells of *E. coli*, strain *B*; ○, cells from a growing culture of *E. coli*, strain *B*; ▲, resting cells of *Salmonella typhimurium*, strain *LT* 2

the rate of inactivation (Fig. 2) and depends only on *t*. Thus the rate of mutation is not influenced by the metabolic state of the cell. This is consistent with the hypothesis that the mutational effect of nitrous acid on living bacteria is direct, that is to say, due to the conversion of adenine, guanine and cytosine present in the deoxyribonucleic acid into hypoxanthine, xanthine and uracil.

(5) From 600 auxotrophic colonies which arose from bacteria plated directly after contact with nitrous acid, none was sectored even with survival rates higher than 5×10^{-1}, nor did any contain wild-type cells. This is contrary to the results of work[4] with phosphorus-32 incorporated into living bacterial cells; in which case the mutagenic effect of disintegrating phosphorus-32 gave cells which formed colonies composed of auxotrophic and prototrophic sectors. The lack of sectored colonies after treatment with nitrous acid, together with the double-hit type of the mutation curve, leads to the conclusion that in order to cause a mutation which is detectable under the experimental conditions applied, nitrous acid must affect both strands of the double-helix of the deoxyribonucleic acid molecule.

I am much indebted to Prof. G. Schramm and Dr. H. Schuster for discussions of this work, a detailed account of which is in preparation.

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BIOLOGY

Effect of Gibberellin on the Termination of Dormancy in Some Seeds

ALTHOUGH the effect of gibberellin on certain growth processes has been extensively studied in recent years[1,2], few reports have been published on the influence of this compound on germination of seeds. Lona[3] and Kahn, Goss and Smith[4] have shown the effect of gibberellin on lettuce seeds. In these, as well as in *Arabidopsis* studied by Kribben[5], gibberellin apparently can substitute for red light necessary for germination of the seeds of these species. Also in the experiments of Bünsow and Bredow[6] the promoting effect of gibberellin on the light-sensitive seeds of *Kalanchoë* is observed. The effect of gibberellin on the revitalization of old seeds is also mentioned[2]; but this is all that has come to our notice.

We have conducted experiments to determine the effect of gibberellin on the germination of seeds of various plants which were collected in the autumn of 1958 in the vicinity of the Arctic Biological Station of the University of Turku at Utsjoki in the northernmost part of Finland (latitude 69° 45′).

Gibberellin (Chas. Pfizer and Co., Inc., New York) was found to exert a marked influence on the germination of the seeds of eight of about the 50 species examined. These eight species are *Luzula parviflora*, *Trollius europaeus*, *Erysimum hieraciifolium*, *Draba hirta*, *Geranium silvaticum*, *Diapensia lapponica*, *Gentiana nivalis* and *Bartsia alpina*.

The germination experiments were performed on filter paper in a Johnson germinator at a temperature of 24° C., and in diffuse daylight conditions.

Because the effect of gibberellin was first observed in the experiments on *Gentiana nivalis* seeds, these have been studied most thoroughly to date. In October 1958 not a single one of 500 seeds germinated in the control experiments (that is, on filter paper), and light as well as cold treatment of 20 days duration had no effect. The results obtained when the seeds were exposed to the action of gibberellin are shown in Table 1. In these conditions the germination took place on the sixth day (Table 1).

Table 1. THE EFFECT OF GIBBERELLIN ON THE GERMINATION OF *Gentiana nivalis*. (PERCENTAGE GERMINATION)

Time of exposure	Gibberellin (per cent)				
	0·5	0·25	0·1	0·01	0·001
1 hr.	100	100	100	1	0
3 hr.	100	100	100	4	0
6 hr.	100	95	97	45	0
8 hr.	90	92	91	70	6
24 hr.	80	95	90	76	22

When the experiments were repeated in February 1959 on seeds that had been stored in the laboratory, none of the control series germinated and the effect of gibberellin on the exposed seeds was the same as in the autumn experiments. In the later part of March the effect of the weak concentrations 0·01 is more effective than in the autumn, the germination percentage being after the treatment of 3 hr. as much as 85 per cent.

Table 2 shows the results of experiments in which the seeds of *Erysimum hieraciifolium*, *Draba hirta*, *Bartsia alpina* and *Luzula parviflora* were exposed to 0·1 and 0·01 per cent solutions of gibberellin.

Table 2. PERCENTAGE OF GERMINATION OF FOUR DIFFERENT SPECIES PRETREATED WITH GIBBERELLIN

	Gibberellin (per cent)	3 hr.	6 hr.	24 hr.	Control
Erysimum hieraciifolium	0·1	85	100	100	25
	0·01	90	100	100	
Draba hirta	0·1	16	20	95	0
	0·01	5	5	10	
Bartsia alpina	0·1	10	80	90	5
	0·01	10	45	85	
Luzula parviflora	0·1	10	10	90	10
	0·01	5	15	90	

In the case of *Trollius*, prolonged soaking in gibberellin solution is necessary to effect germination. After 24 hr. 15 per cent of the seeds exposed to 0·1 per cent gibberellin and 5 per cent of seeds exposed to 0·01 per cent gibberellin germinated, whereas after 48-hr. treatment the respective percentages were 90 and 80.

It is obvious that gibberellin penetrates into the embryo of the *Trollius* seed very slowly. A preliminary treatment with sulphuric acid therefore was given. Seeds pretreated with sulphuric acid for 20 min. germinated to the extent of 70 per cent when they were exposed to a 0·01 per cent gibberellin solution for 3 hr.

The germination experiments with *Diapensia lapponica* were carried out in February 1959. 15 per cent of the seeds exposed to a 0·1 per cent gibberellin solution for 24 hr. were germinated whereas none of the seeds of the control series germinated.

A combination treatment with sulphuric acid and gibberellin gave the best results with *Geranium silvaticum*. The seeds stored in normal room condition germinated very poorly, the germination being less than 1 per cent. Exposure to gibberellin solutions had no effect, and exposure to concentrated sulphuric acid only a slight effect. When, however, the acid-treated seeds were exposed to the gibberellin solution, a very high proportion of the seeds germinated. The most favourable procedure was to treat the seeds first with concentrated sulphuric acid for 30 min. and, after washing, to 0·1 per cent gibberellin for 6 hr. Prolongation of the latter period of exposure to 24 hr. did not increase the proportion of germinated seeds.

No correlation between systematic relations and the effect of gibberellin was established. Seeds of *Gentiana uliginosa* and *G. amarella* from southern Finland and *Luzula sudetica*, *L. pallescens*, *L. spicata*, *L. multiflora* and *Draba incana* did not respond to the treatment with gibberellin. Strains of *Erysimum hieraciifolium* from southern Finland and Poland did not differ significantly from the strains from northern Finland.

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Some Unusual Outgrowths from Secondary Follicles in Soay Sheep

SOME 'plugs' of undifferentiated cells were discovered while the secondary : primary follicle ratio was being determined in preparations of skin from four six-month old Soay lambs. The plugs were found at the sebaceous gland level, and were traced towards the skin surface through the series of sections in order to determine whether they were developing follicles, shedding follicles, or parts of sebaceous glands.

In fact, each plug joined on to the ectal side of a secondary follicle immediately beneath the epidermis and thus arose as an outgrowth. They are thought to be follicle branches that have occurred during the development of follicles[1]. But they were also found in two adults, 3 and 4 years old. The original samples were taken in September 1958; and skin obtained later when two of the lambs were slaughtered unfortunately did not give sufficiently good preparations to show these outgrowths. But a third adult, two years old, sampled in February 1959, had them.

Four of the six outgrowths traced in detail had a lumen extending 60–80μ below their attachment (Fig. 1). This joined the follicle lumen and was either lined or blocked with stratum corneum in the upper part, so that here the outgrowth resembled the sweat duct of a primary follicle. Below this the lumen was blocked discontinuously with pigment. On the termination of the lumen at the sebaceous gland level of the parent follicle the cells of the outgrowth became undifferentiated, usually on the side adjacent to the follicle, but on the opposite side they had the appearance of sebaceous cells for 25–60μ. One outgrowth (in an adult) in fact had an outgrowth of sebaceous tissue in the shape of a sebaceous gland. Below this the cells appeared undifferentiated for the remaining 80–100μ of the length of the outgrowth. Another outgrowth, however, had a bud of undifferentiated cells immediately below the sebaceous portion.

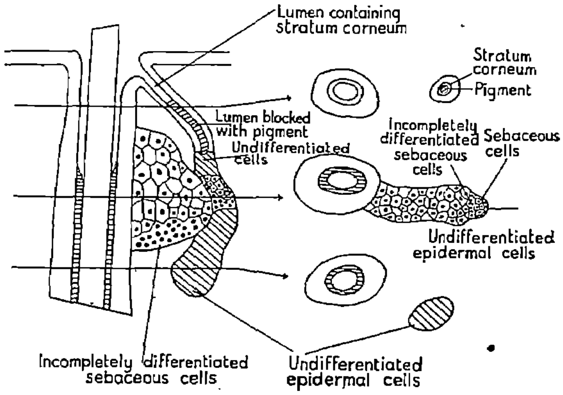
Lumen containing stratum corneum
Stratum corneum
Pigment
Lumen blocked with pigment
Undifferentiated cells
Incompletely differentiated sebaceous cells
Sebaceous cells
Undifferentiated epidermal cells
Incompletely differentiated sebaceous cells
Undifferentiated epidermal cells

Fig. 1. Left, diagram of outgrowth reconstructed from a series of tracings of cross-sections made with a projection microscope; right, some of the cross-sections

One outgrowth (in a lamb) was apparently at an early stage of development in that the cells had an undifferentiated appearance over the whole of its length, and the lumen appeared discontinuously in short lengths. Another (in an adult) was apparently more advanced because it had fragments of inner sheath in the lumen, but there were no traces of fibre.

Most of the outgrowths were apparently attached to the sebaceous gland and sometimes to the outer sheath of the parent follicle, and one was attached to the outer sheath of another follicle. This attachment does not seem to be close, however, but has arisen only from the contact of undifferentiated tissue. At the level of the contact with the sebaceous gland the undifferentiated tissue was inconspicuous, being confined to a narrow strip at the edge of the gland, and in horizontal section there was little to show that the sebaceous gland was other than normal.

Most of the fibres of the Soay are pigmented, and although the outgrowths were frequently pigmented it was noticed that the fibre of the parent follicle was often the only non-pigmented one in the group. This suggested that the growth of the fibre had become less vigorous. The percentage of secondary follicles with these outgrowths ranged from 1 per cent in one of the adults to 23 per cent in one of the lambs. From Table 1 it will be seen that as the percentage of outgrowths decreases, the ratio of mature secondary follicles to each primary increases.

Table 1

	Lambs				Adults	
Percentage of secondary follicles with outgrowths	31	27	20	10	6	1
Mature *S/P* ratio (S_F/P_F)	2·47	2·61	2·99	2·88	3·6	4·64

These outgrowths are thought to have no relation to the outgrowths called capsules[6], which are now thought to be milia (benign tumours). Their appearance near the skin surface suggested that they were sweat glands, and it was thought that their parent follicles may have been intermediate between primary and secondary follicles as described by Burns[2]. However, the outgrowths bear much resemblance to developing follicles; they are very similar in appearance to the developing follicle shown in ref. 3, Fig. 23, and they are on the same side of the follicle as the follicle branches of Hardy and Lyne.

The chief way in which they differ from the developing follicles in fœtal skin of the Romney breed[4] is that the lumen joins the follicle lumen and contains much stratum corneum. The comparable part in a developing follicle, the hair canal, does not open to the surface until the wool fibre pierces the epidermis. In addition, the outgrowths are clearly much retarded when compared with normal developing follicles. Some other skin from a Soay lamb at birth showed many developing follicles, and the *S/P ratio* was already approaching the adult value[5] of about 5/1. Possibly the evidence which suggested most strongly that these outgrowths represent developing follicles comes from the trend in Table 1, in which the *S/P* ratio of follicles with fibres increases as the proportion of outgrowths decreases.

The attachment of the outgrowth to its parent's sebaceous gland seems to be abnormal. But this may throw light on the development of sebaceous tissue because it was always at the level of the parent's sebaceous gland that the cells of the outgrowth became sebaceous-like. It may be that here the undifferentiated cells are under the influence of an organizer from the parent's sebaceous gland which leads to their development into sebaceous cells.

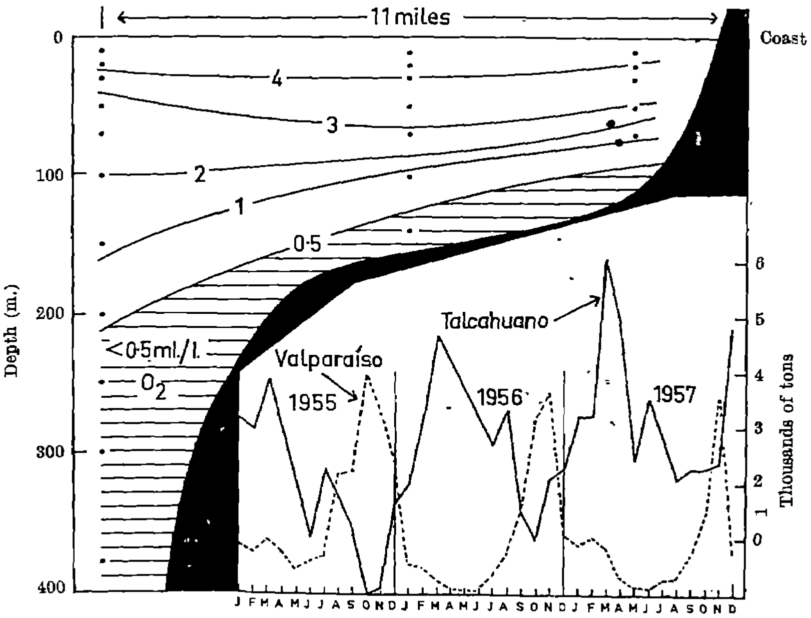

Fig. 2

Fig. 1

I wish to thank Prof. T. Grahame of the Royal (Dick) Veterinary College, Edinburgh, for providing the material for this study, and Miss M. M. Vickers and Miss R. G. Jasper for their technical assistance.

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Relationship between the Hake Fishery and a Southerly Sub-surface Return Flow below the Peru Current off the Chilean Coast

A COMBINED hydrographic and biological investigation has been launched jointly by the Department of Fish and Game of the Ministry of Agriculture of the Republic of Chile and the Technical Foreign Aid Program of the Federal Republic of Germany in order to find possible relationships between the migration and behaviour of fish and the changing hydrographic conditions off the Chilean coast.

The hake, *Merluccius gayi gayi* (Guichenot), is the most important fish to the economy of Chile. More than 50 per cent of the total landings of all species consists of hake. The main trawling grounds are the banks at a depth of 100–150 metres between Papudo (lat. 32° 30′ S.) and the Gulf of Arauco (lat. 37° 15′ S.). Since the continental shelf is very narrow along the Chilean coast, the hake fishery takes place within 10 miles of the shore line. The fish are caught mainly off Valparaiso, San Antonio and Talcahuano. In the northern zone of Valparaiso area, the best fishing occurs during the months September–December, with a steep maximum in the catch statistics in October or November. A sharp drop of the catches to almost zero follows after December. In the Talcahuano area we find moderate catches throughout the year but a pronounced maximum in March (Fig. 1). The yield in the San Antonio area is intermediate. It seems that the stock of hake migrates successively from the northern area of Valparaiso southward, and later in September back to the north.

A preliminary hydrographic survey, carried out off Valparaiso in February 1959, shows extremely interesting results with regard to the oxygen of the water which covers the hake fishery banks (Fig. 2). The oxygen content of the water in an intermediate layer between 100 and more than 380 m. depth (possibly deeper, but no more wire was available) is between 1·0 and 0·4 ml./l., which suggests that the hake has been pushed southward by the lack of oxygen in the water.

By means of salinity and temperature sections off Peru and northern Chile, Gunther[1], proved the existence of a sub-surface return flow below the Peru Current at a depth between 200 and 400 m. Since plankton production in the Peru Current is very high[2], the decomposition of organic material, which sinks into the return flow beneath, apparently causes great depletion of oxygen in this layer. Similar conditions have been found in the north-east Pacific[3].

In Chilean waters there is only Gunther's work, based on the temperature and salinity observations obtained during the cruise of the *William Scoresby* in 1931. We do not know how far this oxygen-poor water extends to the south, how far offshore it extends to the west, and how deep it is. According to the salinity sections drawn by Gunther[1], it seems that this sub-surface current is pushed towards the coast by the effect of the Coriolis force. By changes of some kind in the hydrographic or meteorological conditions, this water covers the hake-fishery banks at certain times of the year, affecting the migration of the hake, and consequently determining the yield of the fishery in the three zones.

The investigation will be continued and a detailed report published later elsewhere.

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Life-Span of Rat and Mouse Erythrocytes in the Rat–Mouse Chimera

THE secondary disease observed in irradiated animals treated with foreign bone marrow is of general interest and importance. The basic question which remains unanswered is whether immunologically competent cells in the chimera originate from the donor, the host, or a combination of both. Erythrocyte life-span studies might be expected to throw light on whether this secondary reaction, in so far as it is reflected in red cell survival, is of host or of donor origin.

Nine $(C57 \times 101)F_1$ female mice that survived 60 days after 900 r. of X-rays (LD100/20 days) and an injection of Sprague–Dawley rat bone marrow (55×10^6 nucleated cells/mouse) on day zero were transfused intravenously with 0·2 ml. of a 45 per cent suspension of chromium-51-labelled red blood cells in saline. Four mice were given labelled isologous erythrocytes and five were given labelled rat erythrocytes; blood was pooled from normal donors for each group. The activity of chromium-51 in circulating blood measured at 24 hr. was taken as 100 per cent, and measurements were made at intervals for 7 weeks. 25 days after the transfusion of labelled cells these animals had essentially 100 per cent rat erythrocytes by the mannitol test[1].

The level of activity of chromium-51 is plotted against time in Fig. 1, and it can be seen that the rat cells disappeared more rapidly in the chimera than did the mouse cells. The latter followed a normal life-span curve for this strain. The curve for rat erythrocytes is intermediate between that for rat cells in the normal rat (maximum life span: 60 days) and that for rat cells in the normal mouse (maximum life span: 4 days) (Smith and Tohá[2]). It was found by Smith and Tohá[2] that rat cells from a rat–mouse chimera survived in normal recipients like cells from a normal rat.

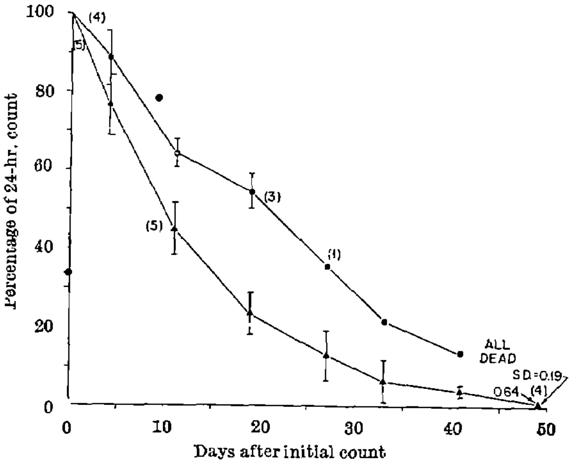

Fig. 1. Disappearance of chromium-51 activity from the circulating blood of rat–mouse chimeras transfused on day zero minus one with either mouse (upper curve) or rat (lower curve) labelled erythrocytes. Number of surviving animals in each group is shown in parentheses at three time points on the curves. Standard deviations are indicated by vertical bars at each point plotted

It is clear from these preliminary results that the long-term heterologous chimera, although 100 per cent of its circulating erythrocytes are of rat origin, provides an imperfect environment for rat red blood cells. On the other hand, the presence of active rat hæmatopoietic tissues in such a host does not influence the survival of transfused mouse erythrocytes. This study therefore provides no evidence of an active rat immune system. Whether the accelerated destruction of rat cells reflects a recovering host immune system, as is clearly indicated by the findings of Gengozian *et al.*[3], or only the foreign biochemical and physiological environment of these heterologous cells cannot be answered by these data.

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Assortative Mating and Reciprocal Difference in the Blue–Snow Goose Complex

THE lesser snow goose *Chen hyperborea* and the blue goose *Chen caerulescens* are maintained as good species by the standard taxonomic works[1] though the morphological difference between them is confined to colour of plumage. The geographical distribution of the two is different. The snow goose ranges through Siberia, western Canada, the Hudson Bay area and Baffin Island; west of Banks Island the populations are unmixed. To the east, however, most populations contain some blue geese and in the Bowman Bay area of Baffin Island there exist several populations in which more than 90 per cent of the birds are blue. Where the populations are mixed, interbreeding between the two occurs, and the progeny produced are viable, fertile[2] and phenotypically distinct[3]. This has led some authorities[4] to consider the two forms to be polymorphs of one biological species. This communication is concerned with observations made by one of us (F. G. C.) on breeding behaviour in the mixed Boas River population, and for convenience the terms blue and snow are used in a purely descriptive sense. Table 1 shows the observed and expected (random mating) distribution for three

Table 1. OBSERVED AND EXPECTED DISTRIBUTION OF DIFFERENT MATINGS IN A MIXED BLUE AND SNOW GOOSE POPULATION

Type of mating	Two snow birds	Two blue birds	One blue, one snow	Total
No. observed	373	64	83	520
No. expected	330·4	21·4	168·2	520

types of mating: (1) both snow birds; (2) both blue birds; (3) one snow and one blue bird in a random sample of 520 breeding pairs from the Boas River population in 1952.

The χ^2 value for the deviations from expected is very large, 133·45, which for 3 degrees of freedom indicates a probability of less than one in a thousand of obtaining such a result by chance alone.

This is strong evidence for the existence of positive assortative mating in mixed populations and this is in agreement with earlier work[5,6].

In our study, however, the reciprocal matings snow × blue and blue × snow were distinguished. Table 2 shows for the 83 mixed pairs the observed and expected distribution.

Table 2. OBSERVED AND EXPECTED DISTRIBUTION OF THE TWO RECIPROCAL TYPES OF MIXED MATING IN A MIXED BLUE AND SNOW GOOSE POPULATION

Type of mating	Snow (♀) and blue (♂)	Blue (♀) and snow (♂)	Total
Observed	54	29	83
Expected	41·5	41·5	83

The χ^2 value for the deviations in this case is 7·52 for 1 degree of freedom. The probability that this is the result of chance alone is less than one in a hundred. We may feel, therefore, confident that the incidence of the two reciprocal matings is really different in this, and presumably in other mixed populations, and it is of some evolutionary interest to speculate as to possible reasons for this. One reason may be that the sex ratio is different in the two phases. There are no indications that this is in fact true, but a sex ratio disturbed in the direction of relative female preponderance in snow geese and in the direction of relatively more males in the blue geese might give the effect observed.

A more likely hypothesis is that the mechanism governing resistance to unlike-mate choice more readily breaks down in one type of pair formation than in the other. This might involve different levels of receptivity on the part of the two female types, different levels of sexual drive on the part of the two male types or both. Only a study of the long-term dynamics of the mating barrier would tell us what factors are involved, but from other evidence it is possible to infer what might be happening. The frequency of the blue phase is increasing in all known mixed populations and more populations are becoming mixed; in the Darwinian struggle for existence it seems that the snow phase is losing to the blue and what is observed at present is a transient polymorphism (which may, of course, later become balanced).

Among other things one component of the selective advantage enjoyed by the blue phase may be sexual in that blue males find it easier to obtain an unlike mate than do snow males. The situation is complicated by the fact that the majority of blue birds involved in mixed matings are white-bellied (that is, heterozygous at the principal genetic locus governing difference in colour). This then implies that hybrid males may mate more easily than pure blue males, and in an evolutionary sense this might be a factor in promoting a balanced polymorphic system in the species-complex but equilibrium is so far from being attained than further speculation upon this point seems unwarranted.

Whatever the mechanism underlying the reciprocal mating difference, it is clear that it depends upon factors other than those which are responsible for assortative mating as such, although this is in itself a matter of considerable interest. Further study should show how far mating preference is a result of family structure[4], imprinting[7], pleiotropy of colour genes or more complex genetic systems, and will, it is hoped, contribute towards a better understanding of the taxonomic problem.

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Hæmoglobin and the Habitat of the Harpacticoid Copepod *Elaphoidella gracilis* (Sars)

HÆMOGLOBIN has only recently been found in free-living copepods. Munro Fox[1] found that certain mud-dwelling harpacticoids contained this respiratory pigment, while allied species living in moss or open water lacked it. The correlation between hæmoglobin and habitat can now be extended by the discovery of hæmoglobin in *Elaphoidella gracilis*, a species which inhabits burrows in decaying aquatic vegetation. The red pigment in this species is easily visible under the microscope, and its identity was established spectroscopically.

Elaphoidella gracilis is not very often recorded because of its burrowing habits. Gurney[2], writing of its seasonal occurrence, says "the capture of it is so capricious that nothing certain is known". Donner[3] regards it as a summer form, but I have found this species to be present and active in the Long Water at Hampton Court throughout the whole of the last winter.

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Role of the Supra-œsophageal Ganglion during the Early Stages of Caudal Regeneration in Some Errant Polychætes

THE importance of the nervous system in annelid regeneration has been realized for some years[1], and it has emerged that, at least in lumbricid oligochætes and nereid polychætes, the supra-œsophageal ganglion secretes hormones that are essential for regeneration[2-4]. Durchon[3] showed that if the supra-œsophageal ganglion of three species of nereid is removed regeneration is retarded. Hubl[4] discovered that, in lumbricids, extirpation of the supra-œsophageal ganglion at the same time as a number of posterior segments is removed totally inhibits posterior regeneration, but that if the brain is removed 24–48 hr. after the posterior segments are amputated then posterior regeneration proceeds at the normal rate. There is thus a brief critical period during which the brain exerts its influence in initiating regeneration. Since Durchon extirpated the brain of his animals 24 hr. after amputating the posterior segments, it is not clear if the difference between his results and those of Hubl represents a real difference between lumbricids and nereids, or if it is due to the difference in experimental procedure.

Durchon's experiments have been repeated on *Nereis diversicolor*[5], and it has been found that extirpation of the supra-œsophageal ganglion 24-hr. before amputation of a number of posterior segments totally inhibits the proliferation of new segments, though one-third of the animals regenerate a pygidium. If the ganglion is extirpated 72 hr. after amputation of the posterior segments, regeneration is retarded, but not prevented, and 16 per cent of the animals proliferated 1 segment during the 30 days the experiment was continued. During this time, control animals regenerated between 1 and 11 segments (average 4).

The events occurring in the regenerating tip, the brain and the blood vascular system during the five days following the loss of posterior segments have been followed in more detail in *Nephtys cirrosa* and *N. hombergi* (members of the Nephtyidae, a family of polychætes closely related to the Nereidae).

During this period the wound is closed and, after an initial stage of dedifferentiation, blastema-formation and regeneration begin. Between the first and second days, muscle cells begin to dedifferentiate, and there is an accumulation of cœlomocytes at the wound. Cell division does not occur until the second day and is then confined to the gut epithelium and to a few dedifferentiated mesenchyme cells. By the third day, mitoses are common in the preterminal part of the nerve cord, and it is not until the fourth day that mitoses occur in the tip of the nerve cord and in the epidermis.

Within 6 hr. of amputation of a number of segments, neurosecretory cells in nucleus S[6] of the supra-œsophageal ganglion become active. After about 48 hr. the secretory cell-nucleus becomes very angular, the cytoplasm of the cell is vacuolated and appears to be depleted of its secretion. No more than one or two cells on either side of the ganglion are involved. Cells in ganglionic nucleus Z show visible signs of secretory activity 24–48 hr. after the loss of the segments. These cells become depleted of their secretion within a further 24 hr., but others in the same ganglionic nucleus start to secrete and replace them. A few cells in this nucleus contain neurosecretory material even in worms that have regenerated 12 or more segments. The secretion produced by both sets of cells migrates along the axons and those from ganglionic nucleus Z run to the cerebro-vascular complex at the base of the ganglion where neurosecretory material is released into the blood vessels[7].

Neurosecretory material is taken up by blood corpuscles[7], and these increase enormously in number during the early stages of regeneration. Initially, no more than one or two can be counted in the blood vessel beneath the brain; their numbers begin to increase about 12 hr. after amputation, and by the fifth day nearly 70 can be counted in the same length of blood vessel. A comparable increase in the number of blood corpuscles can be detected in vessels near the regenerating tip.

Detailed accounts of this work will be published elsewhere.

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The Proposed Biological Term 'Pheromone'

Karlson and Lüscher[1] have recently proposed the term 'pheromone' for a class of substances which, while resembling hormones in some respects, cannot be included among them because they are not of an endocrine origin. It is claimed that the latter part of the proposed word is derived from the Greek *hormōn* (which should properly be *hormān*), meaning 'to excite'. This is not so. It was apparently the intention of the authors to find a term which, while being derivable from *hormān*, bore little overt resemblance to the word 'hormone'. This they achieved by the improper expedient of dropping the letter 'r', thus mutilating the root of the Greek word. It should be a principle, when a scientific term is derived from classical origins, that the term must by its structure be traceable to those origins. In the case of the word 'pheromone' that principle is not observed: there is no structural clue to its derivation from *hormān*. Indeed, the only Greek verb (apart from *pherein*) which might conceivably be involved in its ancestry means 'to swear'.

It would be an etymological improvement to re-instate the missing 'r', making 'pherormone'. If this too closely resembles 'hormone', an alternative would be to abandon Greek and use the word 'transcitant', derived from the Latin *trans* and *citare* (to excite). The approximate meaning, as well as the derivation, of this word is readily deducible—an advantage not shared by 'pherormone'.

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It was our aim to introduce, for a class of substances, a scientific term of international usefulness. Based on a clear definition, it should be a short word easily pronounced in many languages. This is not the case with 'pherormone'. It must be admitted that the derivation of 'pheromone' from *hormān* is questionable. We would therefore not insist on it; but we regard the ending 'mone' as a proper suffix which is used in hormone, gamone, termone and pheromone.

The alternative proposal 'transcitant' is regarded as unfortunate. Its translation would refer to a neurohumoral transmitter substance rather than to a pheromone. The exciting activity is only one of their possible actions. Furthermore, the parallelism to hormone, gamone, etc., is entirely lost.

P. Karlson
M. Lüscher

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